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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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SUMMARY OF RECENT ABSTRACTS.*

IV. TRYPANOSOMIASIS.

African Trypanosomiasis.

Epidemiology: Transmission.

MacGowan (p. 106) reports that in one district on the north bank of the river Gambia the incidence of human trypanosomiasis has fallen greatly in recent years, as a result of treatment carried out at a dispensary. On the south side the people are reluctant to receive treatment, and the infection rate remains as high as before.

Diaz-Varela (p. 547) gives an account of human trypanosomiasis in Fernando Po, where the campaign against this *Trypanosoma gambiense* infection was begun in 1928. The disease still persists.

Nash (p. 653) notes that some West African streams are choked by the palm *Raphia*, which provides very suitable conditions for *Glossina tachinoides* and which is much used for roofing. The cutting of the poles is therefore a danger in that it entails close contact with the fly. Nash states that a law has been made prohibiting the cutting of the poles except during the first fortnight of each 3-month period; if this is obeyed it will mean that a whole generation of flies (and their infection) will die out between two successive cutting periods.

Nash (p. 653) shows that when streams in West Africa become dry, the remaining *G. palpalis* tend to concentrate round the water holes dug in the dry river beds. These are much frequented by the people, and the danger of infection is evident. A few flies may infect many persons in such circumstances.

Chorley (p. 463) reports a heavy concentration of *G. morsitans* in Portuguese territory near the border of S. Rhodesia, and the presence of *G. pallidipes* in the Wankie district. Animal trypanosomiasis appears to be increasing, and human cases are reported for the first time in one area.

Vanderplank (p. 1010) has compared the attractiveness of certain animals for *G. pallidipes*. Dog, ox and porcupine were the most attractive, next domestic pig (and screens), next sheep, goat, man and baboon, last serval cat, lion and jackal. The screens, unscented, or scented by bush-pig, were used for comparison.

van Emden (p. 829) describes a new subspecies of *G. nigrofusca*, which he names *G. nigrofusca hopkinsi*. It is found in Western Uganda.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1944, v. 41. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

Aetiology.

LAVIER (p. 368) discusses at length the classification of the trypanosomes, and the evolution of their morphology. The argument cannot be more briefly stated than in the original abstract, which readers are advised to consult. He holds that all the pathogenic forms have originated from trypanosomes of ungulates which, originally adapted to the posterior station of their vectors, later, when they began to be transmitted by tsetse, adapted themselves to the anterior station and development in a salivary medium. But adaptation to the anterior station is poor in comparison with the good adaptation to the posterior station of their vectors shown by the non-pathogenic mammalian trypanosomes. This is approximately 100 per cent., whereas infectivity of *T. vivax* for tsetse is about 50 per cent., of *T. congolense* is less, and of the *T. brucei* group is very much less.

VANDERPLANK (p. 829) has published a preliminary note of an investigation into the structure of the nucleus of trypanosomes.

PACKCHANIAN (p. 107) gives the results of a number of experiments on the viability of various trypanosomes and leishmania in culture; details should be sought in the original abstract.

WEINMAN (p. 653) has cultivated *T. gambiense* in a modification of the leptospira medium used by Noguchi and Battistini, incubated at 26°–28°C. In this medium the trypanosomes have been maintained alive for 71 days, or, by numerous transplants, for 127 days.

It is known that repeated exposure of trypanosomes to sub-effective doses of acridine compounds leads to resistance to acriflavine and to arsenical compounds. LOURIE and COLLIER (p. 370), however, have shown that exposure of *T. rhodesiense* to mepacrine does not lead to resistance to that compound or to arsenicals, and conclude, therefore, that suppressive mepacrine for the control of malaria can safely be given to men exposed to infection with trypanosomes without risk of development of resistant forms.

Clinical Findings: Treatment.

LINHARD (p. 14) has examined daily the blood of patients with [presumably] *T. gambiense* infections, and concludes that there is no evidence of cyclical appearance of the trypanosomes. Sleeping sickness may be missed if only one blood examination is made, as in routine surveys. His results indicate that examination of sternal puncture material is a more certain method of diagnosis than blood examination.

CHOUMARA (p. 14) has found trypanosomes in the ascitic fluid of a child in West Africa.

SCOTT (p. 733) has investigated the eyes of a series of patients with *T. gambiense* infection. Keratitis was common, but was usually due to trachoma, only in 1 of 42 cases could it be attributed to trypanosomiasis. Irido-cyclitis was found in 7 of 150 cases. Scott advises the testing of vision before each injection of tryparsamide, because of the danger of arsenical optic atrophy; the slightest diminution of visual acuity is an urgent sign that treatment must be stopped.

FULTON and YORKE (p. 15) have examined the therapeutic efficiency of six drugs in trypanosome infections of mice. The paper cannot usefully be condensed and should be consulted in the original. The drugs included tryparsamide, novarsenobillon, diamidines and a phenanthridinium compound; differences in efficiency are noted according to the route of administration employed.

MURAZ (p. 734) reports, not unfavourably, on the value of three arsenical preparations in West African sleeping sickness.

POTTER (p. 370) gives an account of four cases of acute visual impairment after the administration of tryparsamide; this condition has received less attention than chronic affections. In all there was contraction of the visual field, which improved somewhat within a few weeks. The author thinks that this type of accident is probably a result of idiosyncrasy. No contra-indication to tryparsamide had been found at ophthalmoscopic examination before treatment was started, though such examination can guard against progressive deterioration of vision due to the chronic type of tryparsamide reaction. Injections of thiamin, and spinal drainage, have little therapeutic value in these cases.

SANDGROUND and HAMILTON (p. 372) have shown that, in rats, *p*-aminobenzoic acid has great power to detoxify certain pentavalent arsenicals (including tryparsamide) without interfering with their trypanocidal action against *T. equiperdum*. This effect was present if the PAB was given (orally or by injection) at the same time as, or shortly before, the arsenical; when given after the arsenical, however, PAB showed great reduction of protective power. PAB alone is not trypanocidal.

BOMFORD (p. 1008) reports a case, probably of *T. gambiense* infection, in a European from Sierra Leone. Treatment with pentamidine was successful in producing clinical cure and in reducing the cerebrospinal fluid cell count to 4 per cmm., and the protein to 0·03 per cent.

HARDING (p. 1009), in discussing the paper by Bomford (above) reviews his own experience with pentamidine and the more well-known drugs, in 2,000 cases in West Africa. In early cases pentamidine is about as effective as Bayer 205 followed by tryparsamide, but in late cases is much less effective than these drugs. Pentamidine has little value once the central nervous system is affected; the dividing line is around 10–15 cells per cmm. [In comment CORSON points out that protein content may be a more important guide than cell count.] Pentamidine may be given concurrently with tryparsamide, and this system has produced good results, even in late cases. Results cannot be well assessed unless the patient is observed for at least one year.

MCCOMAS and MARTIN (p. 466) report a case of sleeping sickness in a West African soldier who died in status epilepticus after the third injection of pentamidine. Post-mortem examination showed that the infection was of considerable duration.

VAN HOOF, HENRARD and PEEL (p. 928) have investigated the action of pentamidine in the treatment and prevention of *T. gambiense* infection. In treatment their results were not unlike those reported by others—the drug was not satisfactory in late-stage disease. Like Bayer 205, pentamidine apparently has a prolonged action with a slow rate of elimination or excretion. Two volunteers given injections and subsequently exposed every few days to infective bites did not show trypanosomes in the blood for 10–12 months, but no controls were used, and HAWKING comments that these results permit the alternative explanation that the infecting strains may have been feebly pathogenic for man. A prophylactic experiment in certain villages, heavily exposed to infection, indicated some protective action during three months of observation after injection of pentamidine.

FULTON (p. 929) has carried out experiments on the prophylactic action of various aromatic diamidines in mice subsequently inoculated with *T. rhodesiense* or *T. congolense*. The prophylactic effect, which is proportional to the curative index, lasts about 2–4 weeks, and Fulton states that if frequent inoculations of *T. rhodesiense* are made after the drug injections, protection is apparent for 8–24 weeks, but it is due to immunization by the trypanosomes and not to the drug (after the first 2–4 weeks). He criticizes the work of VAN HOOF *et al.* (above) in this sense.

Control.

The Department of Tsetse Research, Tanganyika Territory (p. 460), has issued a report of its activities since 1936. A 7-year programme of work was begun in 1938, but as a result of the war several schemes have necessarily been closed down. Nevertheless, a great deal has been accomplished. The report deals with studies made of six of the eight species of *Glossina* known to exist in the Territory. JACKSON has found that *G. morsitans* as a rule keeps to a restricted ambit, but that there is a slow outward drift of flies which escape and establish themselves in new ambits. *G. swynnertoni* has a greater tendency to disperse, concentrating in the hard pan in the rainy season and spreading outwards in the dry weather. Fire exclusion reduces the numbers of *G. swynnertoni*, especially if trees and thickets in the hard pan areas are felled ; but though the remaining flies are few, the females are still fertilized in normal proportions. LLOYD and GLASGOW note that clearing of vegetation to a depth of about 100 feet from the edge of water causes great reduction in the numbers of *G. palpalis fuscipes*, though it does not interfere with their food supply, and they still breed in the inland thicket. Work has also been done on *G. pallidipes*, *G. brevipalpis* and *G. austeni*, by MOGGRIDGE and VANDERPLANK, and the latter, with POTTS and FORD, has engaged in various laboratory investigations. BAX has made experiments on the senses of smell and sight of *G. swynnertoni*, and many other investigations, details of which must be sought in the original, have been made by the members of this active team of workers.

BAX (p. 463) enunciates a practical policy for tsetse reclamation in East Africa. He notes that in the last 20 years about 1,000 square miles of Tanganyika Territory have been freed from flies, but that in the same period thousands of square miles have become infested. As a result of advances in knowledge made in recent years, " the whole conception and emphasis of tsetse reclamation is changing." He considers in turn the measures which could be taken to clear the various types of country—cultivation steppe, thorn savannah, miombo wooding, the great plains carrying a lace-work of vegetation. The details of his recommendations cannot effectively be condensed, and should be sought in the original. The prospects for large-scale reclamation are good in certain parts of the country, and the author quotes instances in which a relatively small amount of work has opened up large areas, or so reduced the fly population that settlement has been possible. This is an important paper, which must be taken into account in any scheme of tsetse fly control that may be projected.

FAIRBAIRN (p. 12) has reviewed the agricultural problems posed by sleeping sickness settlements in Tanganyika Territory. When inter-tribal war was prevented by European administration the natives left their defensive clearings and tended to live in more scattered, small communities in the bush country, where contact with tsetse was more intimate. This resulted in loss of cattle and, when human trypanosomiasis appeared, in outbreaks of sleeping sickness, which were dealt with by concentration of the people in special clearings. The ultimate aim in these clearings is to provide 16 acres of land for each family, and the people are urged first to produce food crops and later to keep animals. The problems raised by these measures include preservation of soil fertility, and the production of clarified butter, hides and meat for export, to provide the means of paying for transport. These questions are discussed, and the author points out that in this way educational, medical and other facilities are brought to the people.

CHORLEY (p. 269) gives an account of tsetse control operations during 1940 and 1941 in S. Rhodesia where, near the Portuguese border, there has recently been some considerable extension of cattle trypanosomiasis. *G. morsitans* has invaded the area, and in consequence a programme of game destruction has

been undertaken; over 15,500 animals were shot in 1940, and 20,500 in 1941. A large scheme of native settlement was planned for 1942 in an area of fertile, virgin land which at the time was being rendered safe.

The relative proportions of the first and later stages of West African sleeping sickness among cases diagnosed for the first time are regarded by MURAZ (p. 734) as a good indication of the efficiency of the preventive measures in force. Patients with 0–5 cells per cmm. cerebrospinal fluid are in the first stage, those with more than 20 are in the second stage, the intervening proportion being regarded as doubtful. If frequent inspections of the population have been made, early cases will have been diagnosed and cured; if not, these cases will have passed on to the later stages. In the original, Muraz gives details of findings for 1940 in 31 sectors of the seven French colonies; in only four were the prophylactic measures apparently satisfactory. Nevertheless, much good work has been done in spite of war-time difficulties.

Trypanosomiasis of Animals.

FULTON and YORKE (p. 373) have tested certain drugs in *T. congolense* infections of mice. Results should be sought in the original, but it is noted that the two most active substances were a phenanthridinium compound and diamidino dimethyl stilbene; Bayer 205 was inactive.

CARMICHAEL and BELL (p. 373) have treated cattle, infected with *T. congolense*, with 4 : 4′-diamidino dimethyl stilbene. Cure was effected in some animals, but in doses which gave acute fatal poisoning in others.

FUNKE *et al.* (p. 734) report on the trypanocidal value (on *T. brucei* in mice) of certain derivatives of ethylene diamine. These belong to a group of drugs whose trypanocidal action was not previously known, but which show some promise.

TALIAFERRO and OLSEN (p. 15) discuss the protective action of normal sheep serum against *T. duttoni* of mice.

HORNBY and FRENCH (p. 107) have experimented with repellents for animals exposed to tsetse. A pyrethrum preparation appeared to offer some protection against attack by flies under natural conditions, but as far as infection by trypanosomes is concerned, the experiment was inconclusive.

AMERICAN TRYPANOSOMIASIS (CHAGAS'S DISEASE).

Epidemiology: Transmission.

No case of Chagas's disease has yet been reported from the United States, though six species of *Triatoma* have been found infected with trypanosomes indistinguishable from *T. cruzi*. PACKCHANIAN (p. 270) has been able to infect a man with trypansomes from *Triatoma heidemanni* (indigenous to Texas). This man showed typical symptoms of Chagas's disease.

DAVIS (p. 271) has, in similar fashion, produced typical *T. cruzi* infection in monkeys by inoculation into the eye of infected faecal material from North American triatomids.

WOOD (p. 108) has found infected bugs in Arizona, and names two, *Triatoma rubida* and *T. longipes*, as the chief vectors.

MARTINS *et al.* (p. 191), in an account of 25 cases of Chagas's disease found in the State of Minas Geraes, remark that although no acute case was seen in a survey of one area, more than 20 per cent. of the population harboured *T. cruzi*. An account of this survey is to be published later.

MAZZA and ORIBE (p. 375) have found a high proportion of positive results in Triatomidae taken in the Formosa area of Argentina. They have experimentally infected a colt, but do not report natural infection in horses. Man is also infected,

and apart from the finding of *T. cruzi* in man, the authors report positive Guerreiro-Machado reactions in a proportion of persons with signs of cardiac disease. Other human cases are reported by MAZZA and JAUREGUI (p. 375) in the same area.

CHAGAS (p. 374), the son of the man who first described American trypanosomiasis, gives a list of the vectors of Chagas's disease, and of the animal hosts. The latter include dogs, cats, armadillos, squirrel monkeys, a weasel-like animal, opossums, ant-eaters, pigs and bats.

MAZZA and CHACON (p. 108) have found *Panstrongylus geniculatus* infected with *T. cruzi* in Eastern Bolivia, and give the names of other known vectors in the same country.

MAZZA (p. 376) has examined various Triatomidae in Argentina for developing forms of *T. cruzi*. Some were positive, but others, though large numbers were taken, were negative. For details the original should be consulted.

A high infection rate of *Triatoma infestans* has been found in part of Chile by BADINEZ SEPÚLVEDA (p. 549), and a number of human cases were discovered in the same area. Two dogs and a cat were also found to be infected.

ARNOLD and BELL (p. 830) note that *T. rubrofasciata* is found in Hawaii, pointing out that, as a well-known vector of *T. cruzi*, it constitutes a possible health hazard.

MAZZOTTI and LEÓN (p. 192) have succeeded in infecting nymphs of *Triatoma carrioni* with *T. cruzi*.

MAZZOTTI and OSORIO (p. 16) have infected three species of *Ornithodorus* with *T. cruzi*; *O. hermsi* could not be infected in this way.

Aetiology.

DIOS and SOMMERVILLE (p. 829) describe their findings on the inoculation of large numbers of white mice with *T. cruzi* from infected bugs and from man. Many mice proved refractory, but in those which became infected no appreciable difference could be detected between strains from bugs and from man.

SULLIVAN (p. 1011) has shown that *T. cruzi*, present in citrated blood from infected guineapigs, remained viable (and actually multiplied) for 257 days at room temperature. Examination of such blood, including cultivation, is a satisfactory method of diagnosis in man.

SENEKJIE (p. 548) gives an account of the biochemical reactions, cultural characteristics and growth requirements of *T. cruzi*. Details cannot be further abstracted.

TOM (p. 376) describes a modification of the Novy and MacNeal medium for the growth of *T. cruzi*. This cannot be further abstracted; details are given in the abstract.

MEYER (p. 468) has shown that in tissue culture of brain and spinal ganglia of chick embryos, *T. cruzi* invades the nerve cells as well as the other cells of the nerve tissue.

DIOS and BONACCI (p. 468) have failed to infect toads with *T. cruzi*.

DENISON (p. 467) has studied *T. cruzi* infection of rats in relation to reticulo-endothelial blockade.

MAZZA *et al.* (p. 16) have prepared a dialysed filtrate of an emulsion of ground *T. cruzi*, which they have used as antigen for an allergic skin test in Chagas's disease. Injection of this substance into the skin gives rise to an immediate reaction in sensitive persons; the authors give a detailed account of the pathology of the skin in such reactions.

WOOD (p. 192) notes that in 1941, INGMAN found *Trypanosoma vespertilionis* in a bat in California. This trypanosome closely resembles (and may be) *T. cruzi*, and Wood advocates a search for the latter in Central California.

Treatment.

Fulton (p. 377) has found no significant difference between the Bayer preparation 7602 (Ac), which has been used in the treatment of Chagas's disease, and the corresponding I.C.I. synthetic product. In mice infected with *T. cruzi* the therapeutic tests were disappointing; the drug has no action on *T. congolense* or *T. rhodesiense.*

Carmona de la Fuente (p. 549) has treated a patient with Bayer 7602 (Ac); symptoms cleared up but the Machado reaction remained positive.

Charles Wilcocks.

MALARIA.

Buxton, P. A. **Rough Notes: Anopheles Mosquitoes and Malaria in Arabia.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Dec., v. 38, No. 3, 205–14. [21 refs.]

This paper contains a summarized collection of the information available on the geographical distribution of malaria in all the Arab Lands in Asia, excluding Sinai, Palestine, Transjordan, Syria and Iraq, and on the anopheline fauna and malaria vectors.

The information on distribution, being itself a summary, does not lend itself well to condensation and should be referred to in the original. The area is divided into three. In Western Arabia malaria is of patchy distribution but severe where it occurs; the southern part of the coastal belt, the valleys which run westwards from the mountains of the Hejaz, Asir and the Yemen, and Jedda, Wadi Liya, Mecca and Taif are noted as malarious; the upper limit would seem to be as high as 6,600 feet. In Southern Arabia, Aden itself is relatively free from the disease, such as occurs being probably caused by anophelines which have been blown long distances by wind, but low-lying ground liable to flooding and oases in the plains may be malarious. In the hills malaria occurs up to an altitude of at least 5,000 ft. and is widespread in the Western Aden Protectorate and the Yemen. In Central Arabia "oasis fever," which is frequent, is almost certainly malaria. On the north-east coast detailed information is available for Bahrein and Dhahran, in both of which malaria is common, as it probably is along the whole coast.

The following anophelines have been recorded: *Anopheles coustani, A. d'thali, A. sergenti, A. culicifacies* and *A. culicifacies* var. *adenensis, A. arabicus, A. subpictus, A. gambiae, A. turkhudi, A. cinereus, A. multicolor, A. stephensi, A. theobaldi, A. pulcherrimus* and *A. pretoriensis.* Of these *A. subpictus* and *A. theobaldi* are probably errors. There are also doubtful records of *A. macmahoni* and *A. rupicolus.*

Malaria vectors are *A. gambiae, A. culicifacies, A. stephensi,* and possibly also *A. sergenti* and *A. multicolor.* *G. Macdonald.*

Pons, R. Orographie et paludisme, ethnographie et habitation, dans le nord de l'Indo-Chine. [**Orography and Malaria, Ethnography and Housing in the North of Indochina.**] *Bull. Soc. Path. Exot.* 1943, May 12 & June 9, v. 36, Nos. 5–6, 167–73, 17 figs. on 6 pls.

This lucid, though condensed, description of the northern third of French Indo-China is the outcome of a 28 months' stay in that country, during which the author made expeditions aggregating 4,000 kilometres. The area described comprises the whole of Tonking and the northern ends of Annam and Laos

down to 17°N. One-tenth of this large area is composed of the alluvial Red River Delta. The rest is hilly or mountainous, the ranges running mostly from the north-west to the south-east. The delta, apart from a few wooded outcrops, is practically free from malaria. In the middle region there is but little endemic malaria in the open plains, but in the wooded portions the endemicity is considerable. In the high region very high malaria endemicity prevails but its intensity is rather a function of orographic conditions [physical conditions of mountainous areas] than of altitude or latitude. In general, the valleys are heavily impregnated with malaria up to a height of 1,200 metres; the narrower the valley, the more shut-in and wooded it is, the higher the endemicity, but the open valleys are by no means immune, pernicious attacks of malaria being frequent enough even there.

The very complicated ethnography of the region is well described in small space and there are excellent photographs of different racial types. The Thaïs predominate among the numerous races in the middle and upper regions. The Thaïs originated in the Yang-tze valley and were pushed south, where they populated Burma, Siam, Laos, a part of Upper Tonking and the south of China. They have adapted themselves to life in unhealthy valleys, and offer a higher degree of resistance to malaria than other races and groups. At the other extreme are the Miaôs who live at altitudes above 800 metres. Their great susceptibility to malaria makes incursions into the lower valleys extremely dangerous. Alongside the Miaôs live the Hos and the Hounis, Chinese mountain tribes, who possess a similarly low degree of resistance to malaria.

All the various groups of Thaïs live in houses built on piles. The space under the dwelling is often used as a stable; an effective measure of zooprophylaxis.

In the discussion of this paper it was pointed out that the all-important factor to be considered was the distribution of the redoubtable vector *A. minimus*, which retains its partiality for feeding on man even in places where domestic animals and game are abundant. The author replied that the distribution of *A. minimus* determines the ethnographic distribution.

Norman White.

SAUTET, J. & MARNEFFE. H. Contribution à l'étude de l'exophilie de divers anophèles vecteurs du paludisme au Liban et au Soudan français. [**A Study of the Outdoor Resting Places of some Malaria-carrying** *Anopheles*.] *Bull. Soc. Path. Exot.* 1943, July 7, v. 36, Nos. 7–8, 226–9.

The authors report observations on the resting of *Anopheles* of several species in the open, outside houses.

In the Lebanon *A. sacharovi* (*elutus*) has been found several times in caves and holes in trees: there is a considerable daily turn-over, for freshly gorged females may be found. *A. sergenti* and *A. superpictus* have been found in holes in walls, the former at a time when it could not be found in a very malarious village close by. The authors do not indicate the season at which these observations were made.

At Bamako, R. Niger, observations were made in August–September (*i.e.* after the rains, but before the height of the dry season). They had no difficulty in discovering adult *A. gambiae* far from human habitations, particularly in folds in bark of the "fromager" (the silk cotton tree, *Ceiba*). In such places they found adults of both sexes. Some females were gorged, and others were hungry and attacked man. They are in these refuges not only by day but also quite late in the evening. The authors also found mosquitoes of this species in screens made of straw.

They recall the fact that in several parts of the world species of *Anopheles* which are undoubtedly house haunters may be found resting in natural environments. *P. A. Buxton.*

WANSON, M. & BERTEAUX, M. Note sur l'infectivité de l'*Anopheles* (*Neocellia*) *brunnipes* Theobald. [**The Infectivity of** *Anopheles* (*Neocellia*) *brunnipes* **Theobald.**] *East African Med. J.*, 1944, Sept., v. 21, No. 9. 272–3.

Anopheles brunnipes is a mosquito of wide distribution in tropical Africa, but has always seemed to be rare. It was originally described from Léopoldville in 1904, and after prolonged search the authors rediscovered it at the same place in 1942. At Léopoldville the adults are only found in the cool dry season (May to August); they occur in labourers' huts, and are frequently full of blood. In 102 females dissected, four salivary infections were found, but in view of its rarity *A. brunnipes* is not regarded as an important carrier of *Plasmodium*.

Near Leopoldville the breeding places and early stages remain undiscovered. *P. A. Buxton.*

D'ABRERA, V. St. E. **The Eggs of the Ceylon Anopheline Mosquitoes.** *J. Malaria Inst. of India.* 1944, June, v. 5, No. 3, 337–59, 18 figs., 1 pl. & 1 map. [22 refs.]

This article embodies the results of studies of the external characteristics of the eggs of Ceylon anophelines, based on original investigation and a study of the literature. In most cases eggs were obtained in the laboratory from gravid females which laid naturally, though in some cases "wild" eggs found on natural water were used, the species being determined by allowing a proportion, after preliminary examination, to hatch, and by comparison with eggs obtained by dissection from gravid females. This latter method was also used for examination of the texture of the exochorion.

A detailed account is given of the mode of oviposition of *A. subpictus*, *A. barbirostris* and *A. varuna*.

Neither original specimens for examination, nor previous descriptions, were available of the eggs of *A. insulaeflorum* or *A. pseudobarbirostris* which remain unknown, and no additional material was available on which to check previous descriptions of *A. annandalei* var. *interruptus* or *A. ramsayi*.

Eggs of the following species were available and are described: *A. barbirostris*, *A. hyrcanus* var. *nigerrimus*, *A. gigas* var. *refutans*, *A. aconitus*, *A. varuna*, *A. culicifacies*, *A. subpictus*, *A. vagus*, *A. tesselatus*, *A. leucosphyrus*, *A. annularis*, *A. pallidus*, *A. jamesi*, *A. maculatus* and *A. karwari*.

The descriptions of the eggs of *A. aitkeni*, *A. gigas* var. *refutans* and probably also *A. karwari* are original and are given in appropriate detail.

The eggs of *A. hyrcanus* var. *nigerrimus* from Ceylon do not conform in detail to the descriptions given by CHRISTOPHERS and BARRAUD [this *Bulletin*, 1932, v. 29, 136] notably in the consistently lower number of float ridges, while the eggs of *A. barbirostris* agree very closely with the previous authors' description of *A. hyrcanus*. The differences, which have been carefully checked, are far too consistent to be lightly dismissed and it seems probable that confusion has occurred.

A fully detailed description is given of the eggs of *A. varuna*, which differs from that of M. A. U. MENON (*J. Mal. Inst. of India*, 1938, v. 1, 121), notably in that every egg without exception was beautifully and intensely sculptured with polygonal markings distributed over the entire integument. The author considers that considerable confusion prevails and suggests further investigation into the relationship between *A. minimus*, *A. fluviatilis* and *A. varuna*.

A tendency to the occurrence of polygonal markings on the ventral surface of the eggs of *A. culicifacies*, not noted by previous authors, is described.

Eggs from specimens of *A. jamesi* with three banded and four banded palps were examined and consistent differences noted.

In other species the eggs found in Ceylon are similar to those previously recorded and brief descriptions and measurements only are given. The paper includes a key to the eggs of Ceylon anopheline mosquitoes. *G. Macdonald.*

Das Gupta, B. M. & Ganguli, S. K. **Developing Gametocytes and Schizonts of *Plasmodium falciparum*: a Case showing all Stages in the Peripheral Circulation.** *Indian Med. Gaz.* 1944, Oct., v. 79, No. 10, 458–9, 16 figs. on pl.

The case described is that of a young adult, 25 years of age, who was admitted to the hospital in Calcutta in an extremely emaciated condition shortly before death. There was a heavy infection with *P. falciparum*, which was remarkable in that large numbers of gametocytes in all stages of development were present in the peripheral blood, together with numbers of schizonts, the majority of which had been phagocytosed especially by polynuclear leucocytes. The occurrence of developing gametocytes in the blood is most unusual, as these forms are found normally in the internal organs, particularly the bone marrow where, as the authors remark, they can frequently be demonstrated by sternal puncture when absent from the peripheral blood. An excellent coloured plate depicts the developing crescents and phagocytosed schizonts. *C. M. Wenyon.*

Kean, B. H. & Smith, J. A. **Death due to Estivo-Autumnal Malaria. A Resumé of One Hundred Autopsy Cases, 1925–1942.** *Amer. J. Trop. Med.* 1944, Sept., v. 24, No. 5, 317–22.

The hundred autopsies on cases of *P. falciparum* malaria represent 1·6 per cent. of all the autopsies performed in the Gorgas Hospital, Ancon, Canal Zone during 17½ years. Sixty per cent. of all deaths were followed by post-mortem examination.

Deaths from *falciparum* malaria occurred in all months but were somewhat more numerous in May and June and in December and January than in other seasons. Seventy patients were male, 30 female; among the Panamanians the sex ratio was equal. These figures reflect the sex distribution of the races on the Isthmus. The average age of the 100 patients was 22·6 years, but of the 39 Panamanians in the series, 34 were aged 10 years or less. If the Panamanian survives childhood he is unlikely to die of malaria. Peripheral blood parasite density was inadequate as an index of the seriousness of the disease; 29 of 66 patients who died had "light infections." Twelve of these died within 24 hours of admission to hospital despite large doses of quinine. The clinical symptoms and pathological changes associated with shock were recorded in one-third of the patients about whom such information was available. The plugging of cerebral capillaries did not appear to be closely related to the occurrence of the symptoms of cerebral malaria. *Norman White.*

Dähne, G. Zur Frage des Verhaltens der Retikulozyten bei den durch Malaria bedingten Anämien. [**The Reticulocytes in the Anaemia of Malaria.**] *Deut. Tropenmed. Ztschr.* 1944, Feb.–Mar., v. 48, No. 3–6, 49–59, 2 figs.

Very high reticulocyte counts have been recorded in malarial anaemia, which is of the secondary type and therefore predominantly hypochromic.

The author has investigated the changes occurring in the reticulocyte counts during treatment with (1) atebrin followed by plasmoquine; (2) "atepe"

[(Bayer); tablets contain atebrin 0·1 gm. and plasmoquine, 0·005 gm.]; and (3) an "atebrin-like drug." The findings were very similar for all three drugs. Simultaneous estimates were made of the haemoglobin and the blood-sedimentation rate.

The atebrin-plasmoquine treatment consisted of—atebrin 0·3 gm. daily for three days by the intramuscular route; then 0·1 gm. thrice daily by the mouth for three days; and plasmoquine 0·01 gm. daily for four days. [Elsewhere the dose of plasmoquine is stated to have been 0·01 gm. twice daily for four days.]

There were great variations in the reticulocyte count both before and after the treatment; but, generally speaking, in patients with pronounced anaemia there was a sharp increase in the reticulocytes about a week after the treatment was started, a maximum response during the 2nd and 3rd week, and a gradual fall towards normal. In patients who were not anaemic the increase in the count was very slight to moderate.

Step by step with the increase in the reticulocytes there was usually a rise in the haemoglobin, though occasionally there was a fall when the initial percentage of haemoglobin had been high.

The blood-sedimentation rate was initially high in patients with profound anaemia; it fell gradually during, and after, treatment; but in non-anaemic patients the initial rate was low, and not infrequently it rose during treatment. A persistently high sedimentation rate was regarded as suggesting that a relapse was likely to occur.

When iron and vitamin C were administered after the end of the treatment there was usually a further rise in the number of the reticulocytes.

Two graphs illustrate the types of reticulocyte response that were observed.

John W. D. Megaw.

Steinberg, L. D., Kanibolotskaya, E. N. & Karlova, N. S. [**Clinical Observations on the Course of Malaria in Children in Voronezh (Aestivo-Autumnal Period of 1943)**]. *Pediatria.* Moscow. 1944, No. 3, 24–32. 5 charts. [In Russian.]

The authors describe atypical phenomena in the course of malaria observed by them among children of the Voronezh province, which was one of the theatres of war, partly under German occupation, in 1941–1943, and had suffered from an epidemic outbreak of malaria. The present observations were based on 154 cases, of which 91 represented benign tertian, 24 malignant tertian and 5 quartan, while in 34 cases a single examination revealed no parasites, the diagnosis of malaria being based on clinical data. In all these cases the clinical course of malaria was similar, irrespective of the type of infection present. While in half of the patients the paroxysms of fever were typical, in the other half they showed various aberrations. Thus there was continuous fever for 3–5 days, which was unaffected by the usual doses of quinine and acriquine [mepacrine]. The onset of fever was rarely accompanied by rigor, and profuse sweating was rarely observed during the crisis. The duration of the paroxysm, as well as the subsequent presence of parasites in the peripheral blood and the occurrence of early relapses, were suggestive of a relative degree of quinine- and acriquine-resistance in the patients. The atypical temperature curve and drug resistance sometimes resulted in erroneous diagnosis, confusion with typhus fever, which was also prevalent in the country, being especially common. While the splenic enlargement was usually typical, enlargement of the liver was rarely present. In some of the children suffering from alimentary dystrophy the splenic reaction to malarial infection was suppressed. Marked oedema was observed in 25 cases. Among symptoms unusual in children, acute headache, associated with malarial paroxysms, was noted in most of the cases.

The authors also describe the effect of untreated malarial infection upon various concomitant diseases. Observations on the combined course of tuberculosis and malaria showed that the latter was capable of activating the tuberculous process, if the child acquired malaria during the course of the primary infection. Malaria also prolonged the duration of dysentery and pneumonia, while in the case of diphtheria, serotherapy proved to be ineffective. In all these cases the treatment of the concomitant diseases began to progress favourably only after administration of quinine.

The authors are inclined to attribute the atypical symptoms observed by them to peculiarities of the malaria parasites. These might be due to the introduction of virulent foreign strains from Italy (by Italian troops) or from Middle Asia (Uzbek troops). On the other hand, there may have been an increase in the virulence of local strains, owing to the absence of anti-malarial control and treatment as well as to serial passage of the parasites through undernourished debilitated human hosts. *C. A. Hoare.*

Fitz-Hugh, T., Jr., Pepper, D. S. & Hopkins, H. U. **The Cerebral Form of Malaria.** *Bull. U.S. Army Med. Dept.* 1944, Dec., No. 83, 39–48.

In a U.S. Army general hospital somewhere in India, where malaria is highly endemic, 6,059 patients suffering from malaria were treated during a period of six months. Among them were 140 cases of cerebral malaria, 2·3 per cent. of the total. The patients were of two classes, Group A being composed of American officers and enlisted men (half Negro soldiers) and a few American women, and Group B comprising officers and men of an Allied nation. Group A consisted of carefully selected individuals whose nutritional state was excellent and whose health had not been impaired by malaria or other infestations. Men of Group B had been less carefully selected; most had suffered from repeated attacks of malaria and many harboured intestinal parasites. Group A supplied 1,764 patients, of whom two died; Group B 4,295 patients, of whom 38 died. There were 40 cases of cerebral malaria in Group A with two deaths and 100 cases in Group B with 33 deaths. The great majority of cerebral cases were *P. falciparum* infections, but one case in Group A was ascribed to *P. vivax*, and in Group B four (one being fatal) to *P. vivax* and one to *P. malariae*.

The variable symptomatology of cerebral malaria is well described. One patient in Group B had severe hypoglycaemia. Maintenance of blood sugar at a level compatible with life while quinine suppressed the malaria infection resulted in complete recovery. There was strong reason to believe that malaria was the cause of this hypoglycaemia.

In prognosis the association of convulsions with coma is grave; 80 per cent. of such cases ended fatally. If to these symptoms be added a high peripheral blood parasite density, the outlook is all but hopeless. On the other hand a number of fatal cases of cerebral malaria had few or no demonstrable parasites in the peripheral blood.

The great majority of cases of cerebral malaria require one or more intravenous injections of quinine hydrochloride, 0·32 to 0·65 gm. in saline or saline-glucose. The drug well diluted, preferably to 500 cc. or more, is administered slowly. Doses of quinine as high as 3 or 4 gm. each 24 hours for two or three days are recommended, thereafter 2 gm. a day until the patient is out of danger of relapse. In maniacal or convulsive patients, intravenous sodium amytal is most useful. In coma, spinal drainage may be of value. Blood or plasma transfusions may be of great value in cases with anaemia, shock or pulmonary oedema. [Pulmonary oedema is usually regarded as a contraindication for

transfusion ; in such cases, if fluid is needed, LOGAN (*Brit. Med. J.*, 1944, Aug. 5, 181) recommends administration through a Ryle's tube into the stomach.] *Norman White.*

MCGINN, S. & CARMODY, J. T. B. **Cerebral Symptoms in Malaria.** *U.S. Nav. Med. Bull.* 1944, Dec., v. 43, No. 6, 1157–62.

At a base hospital, cerebral symptoms have been the most serious and frequent complication in patients suffering from malaria. Sixteen such cases are described, the most surprising feature about them being that they were all ascribed to infection with *P. vivax.* Three of the 16 patients died. In two of these, *P. falciparum* was found in addition to *P. vivax* ; in the remaining 14, only *P. vivax* was present. Eight of the patients had convulsions ; one had many violent convulsions, recurring over a period of nine days. In others a state of coma followed one or more initial convulsive seizures. Fifteen patients were unconscious for a period of from a few hours to five days, the other dying suddenly in his second convulsion. The intravenous injection of quinine was necessary in 15 of the patients, generally 15 grains in 1,000 cc. of 5 per cent. dextrose solution. One such injection was sufficient in six patients, the others requiring two or more. The post-mortem examination of the fatal cases failed to reveal pigmentation and capillary thromboses in the brain ; two of them were icteric.

A case of quinine sensitivity is reported, which was revealed only after the intravenous injection of quinine had been begun. Complete heart block and ventricular fibrillation ensued after only three grains of quinine had entered the vein. The prompt intravenous injection of adrenaline (1 cc. of 1 : 1,000 solution) averted the threatened fatality. *Norman White.*

KERN, R. A. & NORRIS, R. F. **Liver Involvement in Malaria.** *U.S. Nav. Med. Bull.* 1944, Nov., v. 43, No. 5, 847–58.

Clinical experience, based on the treatment of 1,153 cases of malaria in a hospital ship, impressed the authors with the frequency of involvement of the liver in all types of malaria infection and in all stages of the disease. Enlargement of the liver was noted in 59 of 100 consecutive patients suffering from malaria. The enlargement varied from 1 to 2 to 5 or 6 cm. below the costal margin in the midclavicular line. The frequency of enlargement was higher in *falciparum* than in *vivax* infections. Evident jaundice was rarely noted but the van den Bergh reaction frequently gave abnormal readings. In 16 out of 21 patients with enlarged liver and fever the bilirubin exceeded 0·5 mgm. per 100 cc. of serum. This limit was exceeded in 6 out of 12 patients with enlarged liver but no fever, in 7 out of 16 with fever but no enlargement of liver, and in only 3 out of 12 with neither enlargement of liver nor fever. The results of the bromsulphalein test in 19 patients were in general accord with the van den Bergh reactions. Enlargement and altered function of the liver are as common in the primary attack as in subsequent attacks ; they are not evidence of chronicity. The nature of the liver change is uncertain ; it may be a swelling of the parenchymal cells, with compression of the sinusoids ; malarial pigment may be found in the Kupffer cells. *Norman White.*

METCALF, R. J. & UNGAR, J., Jr. **Relapsing Malaria, Analysis of Cases from the Solomons.** *U.S. Nav. Med. Bull.* 1944, Nov., v. 43, No. 5, 859–70.

The observations recorded concern 250 men who had been invalided back to the United States after having been infected with malaria in the Solomons. Records show that many if not most of these men were originally infected

with *P. falciparum*, but on their arrival in the United States *P. vivax* infections were found in every case and *P. falciparum* was not once observed. The group consisted of individuals almost completely lacking in the ability to acquire an adequate degree of immunity, and the relapse rate was very high in spite of what is generally considered to be very adequate malaria treatment. Atabrine [mepacrine] was remarkably ineffective in the treatment of these cases, though it was given in large doses. The last course of treatment previously received by all but two of these patients comprised 3·3 gm. of atebrin. Large doses of quinine were much more effective. The smallest doses of quinine used were : 15 grains thrice daily for five days ; then 10 grains thrice daily for five days ; then 15 grains daily for six weeks. Little was gained by the combination of quinine and atabrine. There was no evidence that plasmoquine was of value. At first, neoarsphenamine was used in conjunction with quinine. It made the patient " feel better " but had insufficient influence on the relapse rate to warrant its routine use. " The ideal drug for eradicating plasmodia, particularly the latent form recently termed the cryptozoite, may well be found to be a colloidal plasmodicide having a special affinity for the reticulo-endothelial system. At this writing such a compound has been evolved by combining high molecular pectin solutions with various soluble plasmodicides. Toxicity studies are promising but as yet no opportunity for using the substance in experimental malaria has been afforded."

The morphology of *P. vivax* seen in these cases was unusual in certain respects. Multiple infection of red cells was common : double rings were seen in many smears, triple rings in occasional smears, and four rings in a single cell were seen five times. There was no doubt that these trophozoites were *P. vivax* and not *P. falciparum*. Intermediary forms between young trophozoites and adult gametocytes are described. During the examination of hanging drop preparations of malarial blood motile forms were seen free in the plasma. These were rod-shaped and had a highly refractile spherical body which could shift its position from one end of the rod to the other. On impact with a red cell the rod would split in its long axis, the two resultant portions ballooning out to form a perfect ring. It is possible that these forms were merozoites from ruptured red cells.

A very low parasitaemia was capable of producing a severe rigor, and no appreciable increase of parasite density was noted in successive relapses in the same individual. *Norman White.*

LANCET. 1945, Feb. 3, 144–5. **Determination of Plasma Mepacrine. A Note on the Anticoagulant. From the Army Malaria Research Unit.** [Reprinted by kind permission].

" Several methods have recently been published for the determination of mepacrine in plasma (Brodie and Udenfriend 1943, Masen 1943). These authors recommend the use of ' oxalate ' as an anticoagulant, but it has now been found that if ammonium oxalate, or any salt mixture containing ammonia (*e.g.*, Wintrobe's salt mixture) is used as the anticoagulant the amount of mepacrine found in the plasma is greatly increased.

" The mean plasma mepacrine concentration of the patients from each of three hospitals has been determined by a modification of the method of Masen (1943). The table gives the mean plasma mepacrine concentration at the end of 48 hours' therapy—*i.e.* after 1·6 g. mepacrine. It is seen that there was no significant difference between the mean plasma levels of the patients of hospitals A and B, and that neither differed significantly from that of an experimental group of medical students and research-workers who had been given the same dosage under controlled conditions. The mean plasma level of patients from

Plasma Mepacrine of Patients after taking 1·6 g. Mepacrine in 48 Hours.

	No. of patients	Mean plasma mepacrine (μg/l)	SE mean
Hospital A	72	84	± 5
Hospital B	6	96	±19
Hospital C	16	245	±17
Experimental group	6	81	± 9
Hospital C (after changing oxalate) ...	4	88	±10

hospital C was, however, nearly three times as great. The difference was maintained throughout the whole of the therapy course. Wintrobe's salt mixture was used as the anticoagulant at hospital C. On changing the anticoagulant to potassium oxalate similar figures were obtained from this hospital also.

" In-vitro experiments have shown that the increase in plasma mepacrine concentration was due to the ammonia in the Wintrobe salt mixture. The ammonia presumably displaces mepacrine from the white blood-cells which have a high concentration of the drug (Brodie and Udenfriend 1943). It has also been shown that if sodium citrate or heparin is used as the anticoagulant the concentration of mepacrine in the plasma is the same as with potassium oxalate.

" *Conclusions and summary.*—If the anticoagulant used contains ammonia, the concentration of mepacrine in the plasma from subjects receiving the drug is much greater than that observed when the plasma is prepared with anticoagulants not containing it. Therefore ammonium oxalate, or any salt mixture containing ammonia (*e.g.*, Wintrobe's salt mixture), must not be used as an anticoagulant in the preparation of the plasma for mepacrine determinations. Potassium oxalate, sodium citrate, or heparin are satisfactory anticoagulants."

References.

Brodie, B. B. & Udenfriend, S. (1943), *J. Biol. Chem.*, v. 151, 299–317.
Masen, J. M. (1943), *Ibid.*, v.148, 529–39.

Shannon, J. A., Earle, D. P., Jr., Brodie, B. B., Taggart, J. V., Berliner, R. W. *et. al.* **The Pharmacological Basis for the Rational Use of Atabrine in the Treatment of Malaria.** *J. Pharm. & Exper. Therap.* 1944, Aug., v. 81, No. 4, 307–30, 2 figs. [11 refs.]

(1) *The physiological disposition of mepacrine (atabrine) in the body.*

The chief features of this are rapid complete absorption from the gastro-intestinal tract, a low rate of excretion, a low rate of degradation, and a tendency to extensive localization in many organs of the body. In the work described, the mepacrine was extracted by ethylene dichloride and the extract was washed with alkali [Brodie & Udenfriend, this *Bulletin*, 1943, v. 40, 821].

Distribution in the blood :—In the blood, the concentration of mepacrine in the erythrocytes is 1–2 times that in the plasma, and the concentration in the leucocytes is over 200 times that in the plasma. The ratio between the concentration in whole blood and that in the plasma varies considerably at different times, partly because of variations in the leucocyte count, partly because of factors at present unknown. When blood is shed, much mepacrine is released from the leucocytes into the plasma ; consequently, the true concentration in the plasma can be determined only if the blood is centrifuged at high speed directly after withdrawal. About 80–90 per cent. of the mepacrine

in the plasma is bound to the plasma proteins, and only 10–20 per cent. is in true solution in the plasma water; it is this 10–20 per cent. which is presumably in equilibrium with the extracellular fluid of the tissues. Technical reasons make the determination of the concentration in plasma water very difficult;

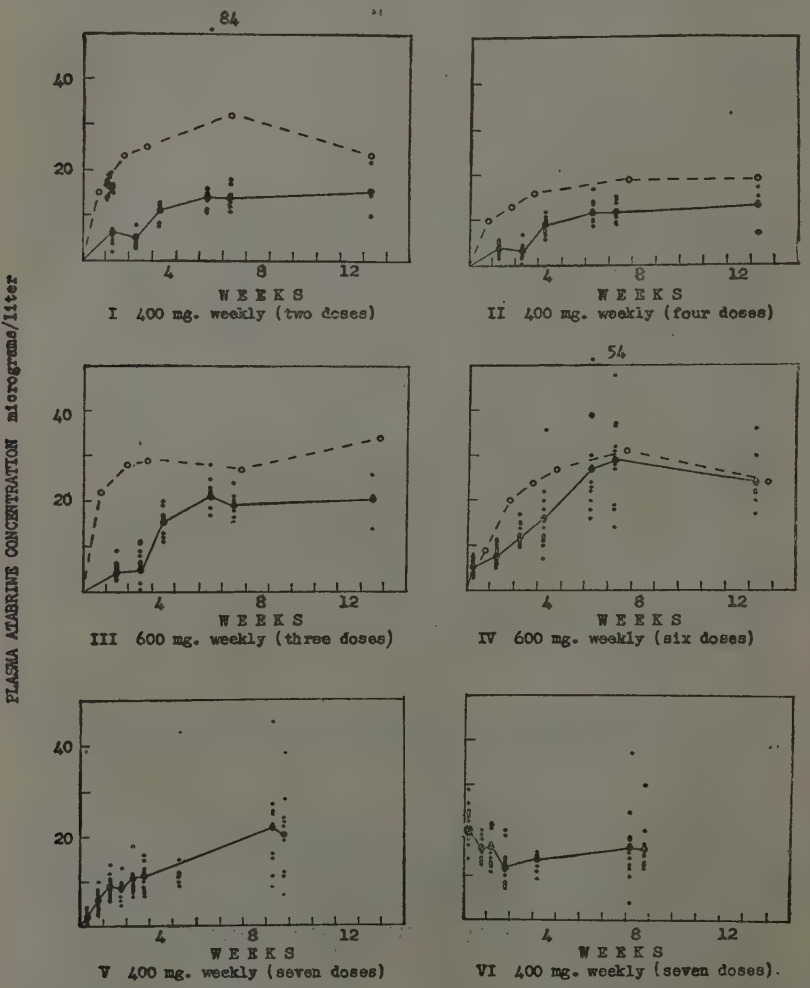

FIG. 1.—Weekly minimal and maximal plasma mepacrine concentrations observed during various regimes of suppressive mepacrine therapy.

The mean weekly minimal concentrations are indicated by large dots, the individual value by small dots. The mean weekly maximal concentrations are indicated by open circles. Note should be taken of the fact that the number of individuals in each group is too small to delineate the mean concentrations accurately. The data do, however, reflect the trend which is to be expected on each of the regimes studied.

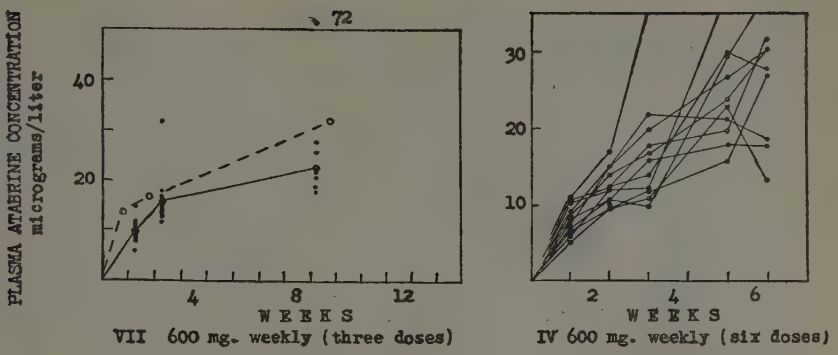

FIG. 2.—Weekly minimal and maximal plasma mepacrine concentrations during the administration of 600 mg. mepacrine dihydrochloride weekly. The symbols used are the same as in fig. 1.

FIG. 3.—The weekly minimal plasma mepacrine concentrations observesd in the individuals of a group receiving 600 mg. of mepacrine dihydrochloride weekly in six 100 mg. doses administered on six consecutive days each week. [Reproduced from the *Journal of Pharmacology and Experimental Therapeutics.*]

consequently the authors recommend that all investigations should be based upon the concentration of mepacrine in whole plasma.

Distribution in the body :—Mepacrine was given to dogs, which were killed after various periods. In a dog killed after 14 daily doses of 20 mgm. per kgm., the concentration of mepacrine in microgram per litre was 0·06 in the plasma, 55 in the muscle, 310 in lung, 571 in spleen, and 1,300 in liver. After single intravenous injections equilibrium took more than four hours to reach. In man there is a similar localization of mepacrine in the tissues, only small fractions remaining in the plasma. Excretion in the dog and in man does not account for more than 1–5 per cent. of the daily dose ; thus patients receiving 300 mgm. daily excreted each day about 5–13 mgm. in the urine and about 10–30 mgm. in the faeces. Degradation or katabolism of mepacrine is also slow, and apparently it depends upon the concentration in the plasma ; on a daily dose, mepacrine gradually accumulates in the body until eventually equilibrium is reached at the point where disposal (degradation plus excretion) balances intake. The level, at which this equilibrium occurs, differs in different individuals.

(2) *Evaluation of mepacrine suppressive therapy by study of plasma concentrations achieved on various dosage schedules.*

Groups, each of about 10 young healthy men, were given mepacrine according to the following schedules :—

(1) 200 mgm. on Tuesdays and Thursdays ;
(2) 100 mgm. on four days of the week ;
(3) 200 mgm. on three consecutive days in the week ;
(4) 100 mgm. on six days of the week ;
(5) 50 mgm. on six days of the week and 100 mgm. on Sundays ;
(6) 200 mgm. on five consecutive days at the beginning of the course (loading doses), and then 400 mgm. weekly as in (5) ;
(7) 200 mgm. on Mondays, Wednesdays and Fridays.

Samples of blood were taken at times when the concentration in the plasma might be expected to be minimal and maximal respectively.

The resulting mean concentrations of mepacrine in the plasma are shown in the accompanying graphs. It will be seen that on these dose schedules, the plasma concentration rises gradually during a period of approximately six weeks and then reaches a comparatively steady level ; this level is lower with a weekly dose of 400 mgm. than it is with a weekly dose of 600 mgm. The degree of protection against malaria presumably depends upon the level of the plasma concentration, so that it is lower in the early weeks than later, and lower with 400 mgm. weekly than with 600 mgm. weekly. The level of plasma concentration finally reached depends more upon the total amount of the drug received per week than upon the exact arrangement of doses within the week. An adequate level of plasma concentration can be reached more quickly by initial " loading " doses (régime 6) than by giving a uniform dosage throughout. There is considerable individual variation in the plasma concentration of mepacrine reached in any given dose-schedule. [It is believed that the plasma concentration of mepacrine required to prevent clinical malaria is about 20 microgm. per litre.]

(3) *Plasma concentrations of mepacrine during several régimes of mepacrine therapy.*

Patients suffering from malaria were given mepacrine according to various régimes, and daily estimations were made of the concentration of the drug in the plasma. The average figures (calculated from the authors' tables) are reproduced below.

In the patients treated by course 2, the plasma concentration was 640–1,100 micrograms per litre after 20 minutes, and 400–800 micrograms three hours later ; two out of six patients showed severe toxic symptoms (depression of respiration and mild convulsions) during this period. Up to 0·4 gm. mepacrine may be injected intravenously without symptoms provided it is given slowly, but the procedure is not recommended for routine use. With course 3, there was much individual variation, but a high concentration was reached within three hours after an intramuscular injection of 0·4 gm. mepacrine ; 0·1 gm. t.d.s. by mouth seldom maintains a plasma concentration greater than that produced by an intramuscular injection of 0·4 gm. With course 4, after several days the plasma concentration tends to become stabilized at 50–100 micrograms per litre. With course 5, most patients remained free from gastro-intestinal disturbances, in spite of the high dosage. In cases where oral administration is not at first possible, a high concentration may be maintained in the plasma by intramuscular injections of 0·4 gm. initial, 0·2 gm. at 8-hour intervals for 2–3 doses, and then 0·2 gm. at 12-hour intervals until oral administration becomes feasible. Following oral administration of mepacrine in the above régimes, no severe toxic manifestations were encountered, apart from several psychoses which may not have been due to mepacrine since the patients were neurosyphilitics. Severe toxic reactions occurred in two patients given mepacrine intravenously, and this procedure is not recommended.

The conventional therapeutic course of mepacrine (course 1 above) is criticized as being unsatisfactory since the plasma concentration does not reach satisfactory levels till the fifth day. In a rational chemotherapeutic régime (as exemplified by the use of sulphonamides), sufficient drug should be administered at the time of diagnosis of a disease to obtain the desired blood concentration and the latter should then be maintained by the serial administration of smaller doses, *e.g.*, courses 3, 4 and 5. The régime recommended for general use is one in which 0·8 gm. is given on each of one or two days, and then 0·3 gm. daily. Unless it is certain that the gastro-intestinal tract is in good condition, the authors recommend commencing treatment by an intra-muscular injection of 0·4 gm., followed by 0·1 gm. orally at intervals during the first day ; in their experience

Course	Dose schedule		Plasma Mepacrine concentration (micrograms per litre)										
			Hours		Days after beginning therapy								
			3	24	2	3	4	5	6	7	10	12	14
1*	0·5 gm. intravenously rapidly plus 0·5 gm. intravenously slowly ...	*range*	390–790	171–425	111–217	—	82–166	—	—	50–117			
		mean	656	261	173	—	121	—	—	86			
2	0·1 gm. t.d.s. orally 6 days ...	*range*	—	12–24	27–43	29–74	40–53	29–75	51–80				
		mean	—	17	33	42	45	55	61				
3	0·4 gm. intramuscularly plus 0·1 gm. by mouth, followed by 0·3 gm. orally distributed throughout the next 12 hours, and then (a) 0·1 gm. b.d.s. by mouth for 5 days or (b) 0·1 gm. t.d.s. by mouth for 5 days	(a) *range*	51–155	34–121	35–121	29–115	33–135	41–143	44–109				
		mean	98	61	66	64	74	69	76				
		(b) *range*	68–138	41–96	47–114	48–104	50–90	43–101	35–81				
		mean	87	57	69	68	67	73	57				
4	0·2 gm. by mouth 4 times in one day, and then 0·1 gm. t.d.s. for 5 days	*range*	—	19–124	25–120	28–102	29–112	40–160	35–121	38–98			
		mean	—	60	63	63	68	70	63	59			
5	0·2 gm. by mouth 4 times a day for 2 days and then 0·1 gm. t.d.s. for 12 days	*range*	—	43–140	47–171	52–135	46–147	50–130	58–105	57–109	44–120	46–127	64–180
		mean	—	73	106	92	89	86	85	81	95	89	100

* In course 1, whole blood concentrations are given as, at the time, the chemical method of measuring mepacrine in plasma was not sufficiently refined. In courses 2 to 5 the plasma mepacrine concentrations are given. The ratio between whole blood concentration and plasma concentration is not altogether constant, but approximately the concentration in whole blood is four times the value for plasma.

intramuscular injection of mepacrine dihydrochloride is not attended by sufficient local discomfort to contraindicate it.

[This is a most important paper laying the foundations for a rational method of administering mepacrine, and it deserves careful study in the original. It should be remembered, however, that the accuracy of estimations of plasma mepacrine is low.] *F. Hawking.*

CHEN, G. & GEILING, E. M. K. **Observations bearing on the Mechanism of the Elimination of Quinine and Atabrine from the Circulation and Tissues.** *J. Pharm. & Exper. Therap.* 1944, Oct., v. 82, No. 2, 120–32, 9 figs. [10 figs.]

The present investigation was undertaken to find out the reason for the rapid disappearance of quinine and atebrin from the circulation or tissues after injection. HATCHER and WEISS [this *Bulletin*, 1927, v. 24, 273], believed that quinine was fixed by the capillaries. In the case of atebrin HECHT [this *Bulletin*, 1937, v. 34, 157], noted that it was taken up by the organs with which it first came in contact and concluded that its location depends therefore on the route of administration. It had already been shown by LIPKIN and by KELSEY and OLDHAM [this *Bulletin*, 1920, v. 15, 127 ; 1944, v. 41, 260], that destruction of quinine in tissues takes place largely by enzyme action. The manner in which atebrin is metabolized has not yet been determined.

In the present experiments chickens were used after partial blockage of the R.E. system by 1 per cent. " norit " [activated carbon] in physiological acacia ; dogs were used with hepatic injury from administration of Cl_4 ; rabbits with leucopenia as the result of exposure to nitro-mustard gas as well as after evisceration, and heart-lung preparations of this animal were also used. By these means it could be determined whether the R.E. system, the blood elements of bone marrow or the capillary wall play a part in the early elimination of the drugs. Estimations of the amount of each drug present in circulation and tissues were made, up to two hours after intravenous administration.

A simple, accurate and rapid fluorimetric method was developed for the estimation of quinine alone in blood and tissues by digesting with 2 per cent. NaOH followed by extraction with ethylene dichloride. In the estimation of quinine along with its fluorescent degradation products, digestion with NaOH was omitted. Suitable standards were employed [for details of estimation the original must be consulted]. Atebrin was estimated by a slight modification of the method of BRODIE and UDENFRIEND [this *Bulletin*, 1944, v. 41, 453].

On injecting quinine or atebrin intravenously in the chick, rabbit and dog, it was found that 95 per cent. had left the circulation within 3 minutes, and the same was approximately true for heart-lung preparations. After one hour the amount of each present was very small. The rate of disappearance was the same in normal animals as after the experimental procedures described above.

Quinine degradation products accounted for 10–12 per cent. of the fluorescent material in the circulation of chicks and rabbits one hour after administration ; 70 per cent. of the quinine injected was destroyed in five minutes in heart-lung preparations, whereas in the case of atebrin 80–90 per cent. of the amount administered was found in the lung up to two hours after injection, the remainder being in the blood and heart. These results show that atebrin was but slowly metabolized in the tissues in question, while quinine was rapidly destroyed by enzyme action, a fact which was confirmed by *in vitro* experiments.

The relationships between the differences in blood levels of the drugs and the times after administration at which they were estimated, suggest that the early rapid removal of these drugs from the circulation is due to an adsorption process

in the tissues. It was concluded that the site at which adsorption takes place is the capillaries, and chiefly those of the lung. *J. D. Fulton.*

HAMMICK, D. L. & CHAMBERS, W. E. **Optical Activity of Excreted Mepacrine.** [Correspondence.] *Nature.* 1945, Feb. 3, 141.

YARYGIN, N. E. & NAGIBINA, N. I. [**On the Treatment of Malaria in Children by Intramuscular Injections of Acriquine and the Rôle of C.S.F. "Towing" in the Treatment of Malaria Cases Refractory to Acriquine-Quinine.**] *Pediatria.* Moscow. 1944, No. 3, 32–6. [In Russian].

Acriquine [=atebrin=mepacrine] therapy is now recognized in the Soviet Union as the standard method of treatment of malaria. Although its effectiveness is beyond doubt, one occasionally meets with complaints that acriquine does not always suppress the paroxysms in children. According to the authors, this impression is due to the fact, that owing to its unpleasant taste, children are reluctant to take the drug or they take an incomplete dose, and furthermore they are subject to vomiting in the course of which the drug is expelled. The authors found that all children suffering from malaria, irrespective of its type, could be effectively treated by intramuscular injection of a 4 per cent. solution of acriquine hydrochloride, in doses corresponding to the age of the patient. The total number of cases thus treated was 410 (398 benign tertian, 9 malignant tertian and 3 quartan).

Among these there were a number (2·2 per cent.) of acriquine-and quinine-resistant cases. In these, injections of 4 per cent. acriquine were combined with treatment by what is described as "towing" of the cerebrospinal fluid, in the course of which a lumbar puncture is done and the first 3–5 cc. of c.s.f. are removed, after which a syringe barrel with a capacity of 5 cc. is attached to the needle and quantities of 4–5 cc. of c.s.f. are alternately withdrawn and injected back from 5 to 15 times in succession. This treatment is said to have resulted in the successful cure of drug-resistant cases. The method itself is based on the views of A. D. SPERANSKY, one of I. P. PAVLOV's collaborators, according to which pathological processes and drug-action are controlled by the nervous system. The "towing" of the c.s.f. is said to represent "a peculiar form of nervous stimulation (massage), which provides the organism with a nervous background required to render the drug effective." *C. A. Hoare.*

FINDLAY, G. M. & STEVENSON, A. C. **Investigations in the Chemotherapy of Malaria in West Africa. II. Malaria Suppression—Quinine and Mepacrine.** *Ann. Trop. Med. & Parasit.* 1944, Dec. 30, v. 38, Nos. 3 & 4, 168–87, 5 charts. [19 refs.]

An interesting historical introduction to this report refers to the experience of expeditions in West Africa, mostly during the nineteenth century. These provided evidence that the administration of cinchona bark or quinine is of value in suppressing clinical attacks of West African malaria. The main body of the report is concerned with observations on the efficacy of mepacrine as a malaria suppressive.

When British troops arrived in West Africa in 1940 all ranks were ordered to take 5 grains of quinine daily. There was some opposition to the measure, based partly on the groundless belief that quinine may cause sterility and dental caries. A daily dose of 5 grains of quinine is not a highly efficient malaria suppressive, but it does prevent clinical attacks in a large number of persons. A daily dose of 8–10 grains is more efficient but it may cause deafness, buzzing in the ears and depression. After changing from quinine to mepacrine prophylaxis, many persons felt more alert and active, both mentally and physically.

Two tablets of 0·1 gm. mepacrine a week were insufficient to suppress malaria. During three weeks of May 1942, the incidence of malaria among 600 men receiving such small doses was 155 per 1,000, as compared with 64·8 per 1,000 among 648 men similarly situated who were receiving each 5 grains of quinine a day. On June 1st the dose of mepacrine was increased to 0·4 gm. weekly, and the test was continued to November 6th. The incidence of malaria among mepacrine takers was 412·4 per 1,000 as compared with 651·7 per 1,000 among troops taking 5 grains of quinine a day. These are the combined results of observations made in Nigeria, Gold Coast, Sierra Leone and the Gambia.

In 1943 three different groups of Europeans in the same area had different suppressive treatments. Each group consisted of from 2,000 to 3,000 persons ; the living conditions of all three were similar. Group A received 5 grains of quinine daily ; group B, 0·4 gm. of mepacrine weekly in two doses ; group C, 0·1 gm. of mepacrine daily except on Sundays. The malaria rate in group A was much higher than in the other two groups : group C had the lowest rate.

In 1943 the whole Command were given 0·6 gm. of mepacrine weekly. The clinical malaria incidence is compared with that of the previous year, when the mepacrine dose was 0·4 gm. a week. The malaria rate per 1,000 men-days exposure to infection fell in all four colonies, from 2·00 to 1·89 in Nigeria, from 2·99 to 1·28 in Gold Coast, from 1·50 to 1·15 in Sierra Leone and from 3·95 to 1·13 in the Gambia. All possible causes of the decreased incidence are considered, and it is concluded that the increased dose of mepacrine was the most potent factor.

Experience has shown that when changing from quinine to mepacrine prophylaxis it is essential to continue 5 grains of quinine daily until at least 0·6 gm. of mepacrine have been taken, otherwise the first two weeks of mepacrine prophylaxis are apt to be marked by a considerably increased prevalence of clinical malaria. It is also essential to begin taking mepacrine 7–10 days before arriving in a hyperendemic zone.

In every case of cerebral malaria that occurred subsequent to the use of mepacrine as a suppressive, there was a history that mepacrine either had not been taken or had been taken irregularly. Mepacrine is much less likely to precipitate an attack of blackwater fever than is quinine. During the year quinine was used as a suppressive there were 122 cases of blackwater fever in the Command ; in the following year, when mepacrine had replaced quinine, there were but 33 cases : the difference was not associated with any great change in the strength of the Command.

Gastro-intestinal symptoms may occur in a considerable proportion of persons during the first two or three weeks of mepacrine suppressive treatment. The symptoms generally tend to disappear ; in about 0·2 per cent. of persons vomiting epigastric pain and diarrhoea persist. No toxic reactions definitely due to the cumulative action of mepacrine had been recorded in patients taking 0·6 gm. of mepacrine a week for periods up to one year. No increased resistance to mepacrine therapy was shown by patients who had taken mepacrine as a suppressive. Some evidence is given that mepacrine may have a sporozoiticidal action in *falciparum* malaria. *Norman White.*

FINDLAY, G. M., MARKSON, J. L. & HOLDEN, J. R. **Investigations in the Chemotherapy of Malaria in West Africa. III. Further Investigations on Treatment with Quinine and Mepacrine.** *Ann. Trop. Med. & Parasit.* 1944, Dec. 30, v. 38, Nos. 3 & 4, 201–4.

In a previous paper the authors had demonstrated the superiority of a large initial dose of mepacrine over the usual daily dose of 0·3 gm. in the treatment of European patients infected with West African strains of *P. falciparum*, and

had shown that mepacrine compared favourably with quinine in the treatment of such patients [this *Bulletin*, 1945, v. 42, 6]. This further contribution records the results of treatment of 80 more patients suffering from *falciparum* malaria, 40 with quinine—30 grains a day for six days—and 40 with mepacrine—0·8 gm. the first day, 0·4 gm. the second and third days, and 0·3 gm. on each of the next three days. Thick blood films were examined morning and evening. The absorption of quinine was verified by Tanret's test thrice daily.

There was a wide variation in the initial parasite counts in these patients; there were more heavy infections in the mepacrine series. There was no significant difference in the response to the two treatments. Mepacrine with a big initial dose can deal with heavy infections by *P. falciparum* as effectively as can quinine. Slight abdominal colic and diarrhoea occurred occasionally during mepacrine therapy but in no case was it necessary to suspend treatment: the patients had all been receiving mepacrine 0·1 gm. daily as a suppressive. All patients on quinine showed a positive Tanret reaction. *Norman White.*

Braun, K. & de Vries, A. **Plasmochin and Quinine as the Cause of Acute Haemolytic Anaemia.** *Harefuah.* Jerusalem. 1944, Dec. 15, v. 27, No. 11. [In Hebrew 219–21. English summary 221.]

Thirlby, R. L. **Hemoglobinuria following Plasmochin Therapy.** *U.S. Nav. Med. Bull.* 1944, Dec., v. 43, No. 6, 1232–5.

Shishlaeva-Matova, L. S. [**Gamostatic Efficiency of Quinoline No. 31 in Benign and Malignant Tertian Malaria.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 6, 22–32. [In Russian.]

The author investigated the duration of the "gamostatic" effect (*i.e.* the power to inhibit the development of gametocytes in the mosquito) of a single dose of 0·06 gm. of "Quinoline No. 31." [See this *Bulletin*, 1939, v. 36, 687; in that Russian paper its formula was given as 6-methoxy-8-diethylamino-methylpropylaminoquinoline (methylene bisalicylate).]

The tests were carried out with *Anopheles maculipennis sacharovi*, which were fed on cases harbouring gametocytes, both before and after administration of the drug. In these experiments there were 23 patients with benign tertian (1,243 mosquitoes) and 28 cases of malignant tertian (1,904 mosquitoes), all of whom were at the same time having a course of treatment with acriquine [mepacrine or atebrin]. In addition to these, six cases of B.T. and seven of M.T. were treated with plasmocide [plasmoquine], for comparison with quinoline. The examination of mosquitoes for developmental stages of the malaria parasites showed that both in benign and in malignant tertian malaria a single dose of quinoline had a pronounced "gamostatic" effect, lasting five days, which compares favourably with plasmocide. *C. A. Hoare.*

Metcalf, R. L. & Hess, A. D. **The Relation of Particle Size to the Effectiveness of Paris Green used in Airplane Dusting for Mosquito Control.** *Pub. Health Rep.* Wash. 1944, Nov. 10, v. 59, No. 45, 1458–65, 3 figs. (2 on 1 pl.).

About two-thirds of the total cost of airplane dusting on the reservoirs of the Tennessee Valley Authority is the cost of the paris green larvicide. Only about 25 per cent. of the amount of paris green released reaches the treatment area; winds and propeller torque dissipate the rest. Studies were therefore carried out to determine whether an increase in the particle size of the dust would increase the efficiency of airplane dusting. The average maximum diameters of particles ingested by first to fourth instar *A. quadrimaculatus*

larvae were 29, 51, 68 and 106 microns respectively. A special paris green was obtained, 84 per cent. by weight of which consisted of particles of from 20 to 50 microns in diameter as compared with 48 per cent. in the standard paris green in use. The use of this coarse dust resulted in a 60 per cent. increase in the amount of dust reaching the treatment area. Field tests with the coarse dust gave a larval kill of 90–100 per cent. It is recommended that specifications for paris green to be used in airplane dusting should be revised.

Norman White.

Dulaney, Anna D. & Morrison, D. B. **On the Preparation and Properties of Antigens from *Plasmodium knowlesi*.** *Amer. J. Trop. Med.* 1944, Sept., v. 24, No. 5, 323–6.

In earlier papers the first author with others has shown that a saline extract of *Plasmodium knowlesi* is a reliable antigen for use in complement fixation tests for malaria [this *Bulletin*, 1941, v. 38, 411; 1943, v. 40, 11]. In the present report the results of using other types of parasite extracts are given. These extracts are: (1) Phosphate buffer extracts of wet and dried parasites; (2) Barbiturate buffer extracts of wet and dried parasites; (3) Solutions of parasites obtained by treatment with barbiturate and NaOH; (4) NaOH solutions of parasites. The method of preparing these four extracts is separately described, as also the technique of their application to the complement fixation test. It was found that phosphate or barbiturate buffer extracts are six to eight times more active than the saline antigens previously employed. The sodium hydroxide solutions are not satisfactory antigens because of their anti-complementary properties. It has been shown that dehydration of phosphate buffer extracts which may be carried out without loss of potency may afford a satisfactory means of storing malaria antigen. Evidence has been produced suggesting that the antigen is a lipid-protein complex, but a carbohydrate factor has not been entirely eliminated. *C. M. Wenyon.*

Jeffery, G. M. **Investigations on the Mosquito Transmission of *Plasmodium lophurae* Coggeshall, 1938.** *Amer. J. Hyg.* 1944, Nov., v. 40, No. 3, 251–63. [16 refs.]

The feeding of the four mosquitoes *Aëdes albopictus*, *Aëdes aegypti*, *Anopheles quadrimaculatus* and *Culex pipiens* on ducks infected with *Plasmodium lophurae* led to the infection of the first three, and of these the anopheline was most heavily infected. When fed on clean ducks the mosquitoes infected only 31 of 52 and of the 31 only three contracted infections which could be termed satisfactory, with 1,600, 3,000 and 11,000 parasites per 10,000 red blood corpuscles. In the other ducks the parasites never exceeded 300 per 10,000 red blood corpuscles. This resistance of ducks to mosquito-transmitted infection contrasts very markedly with their susceptibility to infection produced by blood inoculation. As *P. lophurae* was originally discovered in a pheasant, attempts were made to infect pheasants, known to be highly susceptible to blood inoculations, by means of mosquitoes. The results were similar to those obtained with ducks. It is suggested that the duck is an abnormal host for the parasite and is unsuitable for the satisfactory development of the stages of parasite which must follow the introduction of sporozoites and precede the erythrocytic cycle. Exoerythrocytic stages of development have never been found in hosts of *P. lophurae*, but the fact that infections do follow the inoculation of sporozoites uggests that some must be present but in numbers too small to be detected.

C. M. Wenyon.

COATNEY, G. R. & COOPER, W. C. **The Prophylactic Effect of Sulfadiazine and Sulfaguanidine against Mosquito-borne *Plasmodium gallinaceum* Infection in the Domestic Fowl (Preliminary Report).** *Pub. Health Rep.* Wash. 1944, Nov. 10, v. 59, No. 45, 1455–8.

As a result of experiment, SINTON *et al.* [this *Bulletin*, 1939, v. 36, 925] concluded that the sulphonamide proseptasine had some action as a true causal prophylactic against mosquito-borne infections of the Rumanian strain of *P. falciparum*. It is well known that other sulphonamides possess therapeutic properties in various types of malaria. The present authors have tested the prophylactic effect of sulphadiazine and sulphaguanidine in mosquito-borne infections of *P. gallinaceum*, and this note is a preliminary report of their results.

White Rock chicks, 3–7 days old, were used as hosts. One infected *Aëdes aegypti* mosquito, afterwards shown by dissection to have sporozoites in its salivary glands, was allowed to feed on each bird between the first and second doses of the drug, which was given by mouth twice daily. Blood smears were made of all the experimental birds each day, starting from the sixth, while brain smears were examined after death for the presence of exoerythrocytic forms. In one experiment, 24 chicks were used, each of which was bitten by an infected mosquito. Eight birds received sulphadiazine and eight sulphaguanidine in doses of 1·0 mgm. per gm. of body weight, twice daily by mouth for eight days. The remaining eight birds acted as controls. The blood of the drug-treated birds and of one control was parasite-free at the end of 35 days. The other controls died from infection between the 10th and 16th days. Subinoculation of the blood of the survivors to fresh birds demonstrated the absence of infection, and this was confirmed when the survivors were themselves reinoculated with heavily parasitized blood, as all died from the resulting infection, whereas the course of infection in a chronically infected bird, inoculated at the same time, was unaltered. A second experiment with both drugs yielded similar results with sulphadiazine, but in the case of 12 birds treated with sulphaguanidine, two had parasites in their blood on the 18th and 20th days after exposure, while the others were still negative on the 29th day. A further experiment in which half the above amount of each drug was given as before, for a period of four days, showed that sulphadiazine was effective at this dose, whereas five out of 12 birds receiving sulphaguanidine showed parasites in their blood between the 11th and 18th day, and two of them died, as well as all the controls.

The drug levels attained in the blood by the above dosage were higher than those normally reached in human therapeutic experiments. The authors conclude that sulphadiazine exerted a definite prophylactic action under the conditions of the experiment, while sulphaguanidine was less effective.

J. D. Fulton.

BLACKWATER FEVER.

OLIVER-GONZÁLEZ, J. **Blood Agglutinins in Blackwater Fever.** *Proc. Soc. Exper. Biol. & Med.* 1944, Oct., v. 57, No. 1, 25–6.

Sera from two cases of blackwater fever were examined for the presence of α, β, and cold agglutinins. Both sera contained α and β agglutinins, which were absorbed. Sera were also treated with polysaccharide obtained from *Ascaris suum*. After absorption with A and B agglutinogens and the *Ascaris* polysaccharide, both sera were found to contain cold agglutinins.

The author suggests that in blackwater fever auto-agglutination may result from immunization of the host with a substance in the malaria parasite related

to human isoagglutinogens. There is some evidence that the malaria parasite can behave in this manner, since α and β agglutinins may be increased during the disease.

The possible relationship between the presence of cold agglutinins and the development of blackwater fever is discussed.

[Cold agglutinins were not found in two specimens of sera from blackwater fever cases in West Africa, tested in Britain.] *B. G. Maegraith.*

Rivera Lugo, I. **The Pathology of Blackwater Fever.** *Bol. Asoc. Med. de Puerto Rico.* 1944, Nov., v. 36, No. 11, 461–7, 6 figs. [37 refs.]

TRYPANOSOMIASIS.

Saunders, G. F. T., Holden, J. R. & Hughes, M. H. **Second Report on the Treatment of Trypanosomiasis by Pentamidine.** *Ann. Trop. Med. & Parasit.* 1944, Dec. 30, v. 38, Nos. 3 & 4, 159–68, 1 chart.

In a previous paper [this *Bulletin*, 1942, v. 39, 532] the author reported on the treatment of 14 cases of Gambian sleeping sickness with pentamidine; they comprised "early cases," "central nervous system cases successfully treated," "central nervous system cases unsuccessfully treated," and "difficult advanced cases previously treated with other drugs." In the present paper the results of a follow-up of some of these cases during one to three years are shown, and notes on 12 new cases, also treated with pentamidine, are given. The condition before and after treatment with pentamidine of these and of other cases, making a total of 50, is also shown in a Table.

Pentamidine was given by intravenous injection in doses of from 0·05 to 2 mgm. per kgm. of body weight, the course varying from 10 to 37 injections, usually one a day, but in some cases twice or three times a day.

The only serious immediate effect of an injection was a fall of blood pressure, which might be dangerous; a chart shows observations of blood pressure taken at half-minute intervals after an injection and the effect of a preliminary injection of atropine, which prevented the fall but was followed within a few minutes by an abnormal rise. If the injection was given very slowly, however, the fall was very slight.

The immediate clinical result was very good; of eight earlier cases with a cell count under 30 per cmm., only one had relapsed; of 16 cases with a cell count over 30 or with advanced symptoms 10 showed no improvement, six improved but four relapsed within two years, while two patients, with over 600 cells, were still in good health after over two years.

The author concludes that patients whose cerebrospinal fluid contains less than 30 cells per cmm. are usually cured; when the cell count is above 30 a relapse usually follows treatment, and in very advanced cases the drug is useless. *J. F. Corson.*

Eagle, H. **A New Trypanocidal Agent: V-(p-Arsenosophenyl)-Butyric Acid** *Science.* 1945, Jan. 19, 69–71.

This new trypanocidal compound was found to be the most promising one of a series of phenylarsenoxides which were tested on *Trypanosoma equiperdum* in mice and rabbits [this *Bulletin*, 1945, v. 42, 15]. It is slightly soluble in water, readily soluble in dilute alkali, and neutral solutions of the sodium salt have withstood sterilization in the autoclave, and have afterwards been kept in

sealed ampoules at room temperature for a year without demonstrable change. The chemotherapeutic index [this *Bulletin, loc. cit.*] in mice and rabbits was higher than that of tryparsamide. Cultures of *Schizotrypanum cruzi* were killed within four hours by " dilutions in excess of 1 : 400,000." The author has received personal communications from workers in other laboratories that this compound was found to be effective against *T. rhodesiense* in mice (C. M. Scott) and in *T. gambiense* infections in guineapigs, chimpanzees and man (van Hoof, Henrard and Peel) ; trypanosomes resistant to arsenicals were sensitive to this drug.

In the summer of 1944, it was tried in human trypanosomiasis by Saunders in the Gold Coast, McLetchie in Nigeria, Findlay in the British West African Forces, and by van Hoof in the Belgian Congo. It was supplied as a 2 per cent. solution in ampoules ; the dose varied from 0·25 to 0·5 mgm. per kgm. of body weight (usually doses of 0·8 to 1·5 cc. of the solution were injected). It was given intravenously (sometimes intramuscularly, causing little pain) twice a week, three times a week, or daily, the total number of injections varying from 6 to 24. So far, over 200 patients have been treated and the following conclusions have been drawn : (1) in 800 injections, given in over 100 early cases, no toxic reaction occurred, except that about 2 per cent. of the injections produced nausea and vomiting ; (2) trypanosomes disappear from the peripheral blood and lymph glands within 30 to 60 minutes after the first injection ; (3) early cases can be cured within two weeks by daily injections of about 0·4 mgm. per kgm. ; (4) it is ineffective in clinically late cases and may cause toxic encephalitis in such patients ; (5) it gave good results in a few infected sheep and one horse, but in a few cattle in which it was tried, the trypanosomes persisted [species of trypanosome not stated] ; there is, therefore, reason to think it may be useful in some, but not all, forms of animal trypanosomiasis.

J. F. Corson.

Brauss, F. W. Untersuchungen ueber die Wirksamkeit neuerer Chemotherapeutika gegenüber Nagana-Trypanosomen. [**The Activity of some New Drugs on Nagana Trypanosomes.**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1944, Mar. 30, v. 105, No. 2, 104–10.

These experiments were begun in 1939 and were interrupted by the war. Having found that various sulphonamide compounds had no action on *T. brucei* infections in mice, the author tested a guanidine derivative called " Anticoman " and found that it failed to cure, although it cleared the peripheral circulation of trypanosomes within 24 hours. Surfen was the next compound to be tried ; *in vitro*, it caused morphological changes in the trypanosomes similar to those produced by Germanin, and the trypanosomes became immobile. Experiments *in vivo* showed that a 20 gm. mouse could tolerate 50 mgm. injected intraperitoneally ; doses of 0·05–0·5 mgm. prolonged the life of the infected mouse, while doses of 1–10 mgm. cured it, but a dose of 0·5 mgm., given 24 hours after the infecting inoculation, cured the mouse. If this dose was given later than 24 hours, the mouse died although the peripheral blood remained free from trypanosomes.

Mice were protected by 1 mgm. given 48 hours before the infecting inoculation ; as the drug is quickly removed from the blood no prolonged protective action can be expected.

The trypanosomes of the relapse after a subcurative dose required a larger dose to cause their disappearance from the blood than before.

By giving subcurative doses and making subinoculations, the trypanosomes became more resistant, requiring 1/10 of the tolerated dose instead of 1/50 for cure in the case of untreated infections.

Surfen was also tried against *T. congolense* and *T. equiperdum*; it was effective against *T. equiperdum* and ineffective against *T. congolense*, but for the latter infection treatment with " Congasin-Bayer " is successful. The author concludes that Surfen is a useful trypanocide but it is less effective than Germanin. *J. F. Corson.*

EAGLE, H. & MAGNUSON, H. J. **The Spontaneous Development of Arsenic-Resistance in *Trypanosoma equiperdum*, and its Mechanism.** *J. Pharm. & Exper. Therap.* 1944, Oct., v. 82, No. 2, 137–51, 1 fig. [23 refs.]

A strain of *T. equiperdum* formerly sensitive to phenyl arsenoxides, was found by *in vitro* methods to have become markedly resistant to amino- and amide-substituted derivatives of the parent substance in the absence of all drug treatment. The strain remained sensitive to the parent substance as well as to methyl, chloro or acid-substituted derivatives. The resistance persisted during at least 30 passages in mice and 2 in rabbits. It was definitely established that the change was due to difference in susceptibility of the organisms and not to variation in the drugs used. The nature of arsenic resistance in trypanosomes has been discussed by YORKE *et al.* [this *Bulletin*, 1933, v. 30, 447] and resembles that encountered in the present instance. Various theories have been put forward in explanation of resistance in prepared strains, such as increased tolerance to the drugs, or failure to combine with them. The present authors noted that the living trypanosomes no longer bound certain of the compounds to which they had become resistant, but did bind those to which they were still susceptible, as Yorke *et al.* [this *Bulletin*, 1931, v. 28, 910] had found in the case of a resistant strain of *T. rhodesiense*. HOGAN and EAGLE (*J. Pharm. & Exp. Therap.*, 1944, v. 80, 93) have recently demonstrated that the widely varying toxicity of different arsenicals is related to the degree to which they are bound by the tissues. The theories on the mechanism of selective arsenic resistance are discussed. In inducing resistance in trypanosomes by repeated exposure to an arsenical, the authors suggest that the compound may simply act as a factor which allows a spontaneous variant to become apparent by killing off the more susceptible organisms. In this connexion it is to be noted that resistance is not always specific for the compound producing it. The above theory does not explain, however, why the variant strain in the present instance, having arisen spontaneously, suppressed the parent strain. The view of spontaneous variation is, however, supported by the fact that resistance often becomes maximal soon after it first becomes apparent. *J. D. Fulton.*

BURTT, E. D. **A Note on Variation in Living *Glossina brevipalpis* Newstead (Diptera) with particular reference to a Red-Coloured Form found in Nature.** *Proc. Roy. Entom. Soc. of London.* Ser. A. Gen. Entom. 1944, Dec. 29, v. 19, Pts 10–12, 137.

LEISHMANIASIS.

KHODUKIN, N. I. [**Focal Distribution of Visceral Leishmaniasis in Tashkent for Twenty Years and the Problem of the Reservoir of Infection.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 6, 61–9. [In Russian.]

The author records some of the results of observations on visceral leishmaniasis carried out in Tashkent (Central Asia) during the last 20 years. One of the most remarkable features of this disease is its focal distribution in the town, most cases occurring in localized areas without a tendency to spread outside them, in

spite of the fact that sandflies are uniformly distributed throughout the endemic region. The restricted localization of this disease is attributed to the existence of reservoir hosts, especially dogs, the rôle of which in the spread of leishmaniasis has been suspected for a long time. The data in favour of this view are, on the one hand, aetiological and clinical, and, on the other, epidemiological. Thus, the canine and human parasites (described as *Leishmania canis* and *L. infantum* respectively) are morphologically indistinguishable, have the same antigenic properties and are infective to the same laboratory animals. Moreover, the course of the disease and the pathological changes are the same in children and in dogs, and the areas of distribution of the disease in both hosts coincide. From the epidemiological point of view, man is actually of secondary importance, since the parasites are soon eliminated from the peripheral circulation, whereas the dog constitutes a massive source of infection for sandflies, because in the early stages of the disease the primary lesions are represented by extensive multiple papules situated on the muzzle, while later the infection becomes generalized in the skin. In this connexion it should be taken into consideration that the rate of infection in sandflies depends largely on the abundance of parasites in the skin of the dog, and that the spread of the infection from dog to man is facilitated by the close contact between the two, since they usually share the same dwelling. From these observations it is concluded that the dog is the most important reservoir of infantile kala azar in Central Asia, though there also appears to be some evidence of transmission from man to man, and from man to dog. The rôle of the dog as the source of leishmanial infection is further enhanced by the occurrence in these animals of symptomless infections (in 5·9 per cent.) which may remain inapparent for periods exceeding six months.

It is doubted if sandflies can serve as a reservoir, for the examination of many thousands in the course of about 14 years revealed infected insects only in places where there was a concentration of infected dogs, the insects thus serving merely as vectors. The possibility of rats, mice and lizards serving as reservoir hosts of leishmaniasis was also considered but the examination of these animals has so far failed to reveal the presence of leishmania. *C. A. Hoare.*

MALONE, R. H. & BROOKS, A. G. **Transmission of Kala-Azar in India. The Case against the Sandfly.** *Indian Med. Gaz.* 1944, Oct., v. 79, No. 10, 484–93. [44 refs.]

In this paper the authors argue against the acceptance of the view that kala azar in India is transmitted by *Phlebotomus argentipes*, and this in spite of the fact of successful transmission of the disease to all of five (not seven) volunteers by the bites of infected sandflies. They maintain that there is no real correlation between the distribution of kala azar and that of the sandfly, there being areas, such as Ceylon, where the sandfly occurs while the disease is absent. It is claimed that the whole system of breeding and maintaining sandflies in India for experimental purposes is quite unnatural and that it has resulted in the flies being kept alive longer than their natural span of life, and that this, combined with an artificial diet of raisins, has produced the phenomenon of the blocked fly which has the anterior part of its alimentary tract crowded with flagellates. It is with these abnormal flies, which have no counterpart in nature, that transmission has been effected. Blocked flies have never been met with in the wild state and though naturally infected flies have been discovered their number is too small to support a claim that this fly is the vector.

It is held that *Leishmania donovani* is not a blood parasite but one of the reticulo-endothelial system, and that it cannot, therefore, be regarded as similar to blood parasites which are transmitted by insects. Furthermore, it is not remarkable that an organism should flagellate (not in the sense of flagellation of

a malarial parasite) in an unnatural host. So the parasite of kala azar assumes its flagellate stage not only in the sandfly but also in the bed bug [and it might have been remarked also in the test tube]. As an illustration of the association of a parasite with an unnatural host the production in mice of a leishmania-like infection by the flagellate of the water scorpion is mentioned [in spite of the fact that this claim has been completely disproved since it was first made]. Again, kala azar in India is rarely seen before the age of two. It is commonest in the age period 6 to 20 and is about three times as common in males as in females. These limitations, it is claimed, cannot be reconciled with the sandfly hypothesis.

The authors state finally that sufficient attention has not been paid to the skin, which has been shown to be frequently infected with leishmania. Infections have sometimes spread from one experimental animal to another when living in contact, and it is suggested that the possibilities of the spread of kala azar by way of the skin as a result of abrasions, pathological conditions arising from excessive sweating, or lack of cleanliness, be investigated. The authors write :—

> " We venture to suggest that the supporters of the sandfly theory of transmission have been carried away by the results of laboratory experiments, have not paid sufficient attention to the study of the fly in nature and have ignored or denied the mass of epidemiological evidence which casts grave doubt on the correctness of their theory "

[As the Editor remarks in his note to the paper, this article outlines the many points about the transmission of kala azar in India which are still far from clear and of which further investigation is necessary. Nevertheless it is hardly a refutation of the sandfly theory, which is receiving increasing support from countries outside India for both kala azar and oriental sore.]

C. M. Wenyon.

Sen Gupta, P. C. **The Value of the Complement-Fixation Test in the Diagnosis of Kala-Azar.** *Indian Med. Gaz.* 1944, Oct., v. 79, No. 10, 465–9.

In an earlier publication the author gave an account of the results of a complement-fixation test for kala azar in which an antigen devised by Witebsky, Klingenstein and Kuhn (WKK antigen) was used [this *Bulletin*, 1944, v. 41, 17]. Though it was prepared from tubercle bacilli it had a marked degree of specificity for kala azar. In the present paper a more extensive series of tests have been carried out with a WKK antigen prepared, not from tubercle bacilli, but from more easily cultivated acid-fast organisms, *viz.*, *Mycobacterium phlei* and the so-called leprosy bacilli of Kedrowsky, Lleras, Bayon and Duval. Of 260 cases of kala azar, 241 gave a positive reaction, 16 a doubtful reaction and three a negative reaction. Of 604 cases which might be considered in the differential diagnosis of kala azar, 99 per cent. gave a negative reaction. A positive reaction is obtained in a small proportion of obvious cases of chronic pulmonary tuberculosis. For the early diagnosis of kala azar the test is very useful, some cases giving a positive reaction within three weeks of the onset. The chances of obtaining a positive indication of kala azar are probably greater with this test than by sternal puncture. *C. M. Wenyon.*

Armytage, J. E. & Bolliger, A. **Transmission of Kala-Azar to the Pouch Young of the Common Australian Possum** (*Trichosurus vulpecula*). [Correspondence.] *Nature.* 1945, Feb. 3, 145–6.

The authors infected a 2½ months old common opossum of Australia (*Trichosurus vulpecula*) with kala azar by injecting intraperitoneally 1 cc. of broth washings of a culture of kala azar on N.N.N. medium. The mother was

anaesthetized and the young animal, which was still attached to the mother's nipple, was lifted out of the pouch, inoculated, and replaced in the pouch. About a month later the young animal began to leave the pouch; although eating and moving about, it was weak and underweight, and had a distended abdomen owing to enlargement of the spleen and liver. At 10 weeks a heart puncture was made to obtain blood and the animal died a few minutes later. At autopsy the spleen weighed 8·9 gm. (five times the normal weight), the liver, 26 gm., the left kidney 3·4 gm. and the right kidney 3·2 gm. The blood showed microcytic anaemia with a colour index of 0·69, and marked neutropenia (4 per cent.). Leishman-Donovan bodies were present in a smear of the spleen and in sections of liver and bone marrow, in cultures from the blood, spleen and sternal marrow; the flagellate form of the parasite was seen. The mother was killed three months afterwards and no evidence of infection was found post mortem.

J. F. Corson.

Senekjie, H. A. **American Visceral Leishmaniasis—the Etiological Agent.** *J. Parasitology.* 1944, Oct., v. 30, No. 5, 303–8, 1 fig. [24 refs.]

When, in 1934, Penna reported that the viscerotomy survey, as carried out in Brazil for the purpose of identifying deaths from yellow fever, had revealed the existence of kala azar, it was supposed that this was a special type of the disease caused by a new species of *Leishmania, viz. L. chagasi.* Various arguments in support of this conclusion were advanced but all these have been shown to be unfounded. In the present paper the author reviews this situation and shows that the biochemical, cultural and growth requirements, as well as the bile solubility and the thermal death point, of the S. American parasite are the same as those of *L. donovani.* He concludes, as others have done, that the name *L. chagasi* is a synonym of *L. donovani.* *C. M. Wenyon.*

Kean, B. H. **Cutaneous Leishmaniasis on the Isthmus of Panama.** *Arch. Dermat. & Syph.* 1944, Oct., v. 50, No. 4, 237–8.

In the forty-year period (1904–1944) over 500,000 patients were admitted to the Gorgas Hospital, Panama. Amongst these it has been possible to collect 15 cases of proved cutaneous leishmaniasis, and of these 6 were diagnosed in the year 1943–1944. Most of the cases were in persons who had come to Panama from elsewhere and had resided there for at least seven months. In all cases the disease was acquired in the non-sanitated bush areas. The recognition of six infections in the last year is undoubtedly associated with the recent increase in military activities. Nine of the patients had single sores, while six had multiple lesions. The mucous membranes of the naso-pharynx were involved in one case. The lesions were most unusually seen on the ear or on the dorsum of the forearm, wrist or hand. A striking feature of several cases was a nodular lymphangitis in the areas draining the ulcers. Treatment with antimony potassium tartrate or fouadin was efficacious. The only previous records of cutaneous leishmaniasis in Panama are from case reports of over 30 years ago. In a note to the present paper it is reported that an endemic focus has been discovered in Arraijan, Panama. *C. M. Wenyon.*

Berberian, D. A. **Cutaneous Leishmaniasis (Oriental Sore). II. Incubation Period.** *Arch. Dermat. & Syph.* 1944, Oct., v. 50, No. 4, 231–2. [10 refs.]

In a previous paper [this *Bulletin*, 1939, v. 36, 1035] the author reported that in 35 cases of oriental sore induced by the inoculation of suspensions of flagellates from cultures of *Leishmania tropica*, the incubation period had varied from two

weeks to six months. Other observers who have practised this protective inoculation, have noted incubation periods of three weeks to 11 months, two to 12 months, two to eight weeks, less than a fortnight to more than two months. In the author's experience the incubation period varies with the quantity of the inoculum, the depth of the inoculation and the individual susceptibility. Occasionally the incubation period is prolonged. To illustrate this, three cases are reported. In all three, culture flagellates were inoculated intracutaneously on the left thigh, the lesions being first noted after 18, 30 and 56 months respectively. [For part I of this series see this *Bulletin*, 1945, v. 42, 102.]

C. M. Wenyon.

BERBERIAN, D. A. **Cutaneous Leishmaniasis (Oriental Sore). III. Period of Infectivity of Saline Suspensions of *Leishmania tropica* Cultures kept at Room Temperature.** *Arch. Dermat. & Syph.* 1944, Oct., v. 50, No. 4, 233.

Leptomonads from cultures of *Leishmania tropica* grown on modified N.N.N. medium and suspended in isotonic solution of sodium chloride, will remain alive for seventeen days at laboratory temperatures varying from 15·8 to 38·3°C. The suspension, which was distributed in 0·5 cc. amounts in ampoules, contained approximately 3,350,000 leptomonads per cc. Viability was proved by the production of oriental sore in volunteers (intracutaneous inoculation of 0·1 and 0·2 cc.) and the presence of motile flagellates. The observations were made to meet the need of physicians, in districts distant from laboratories, who require suspensions for purposes of immunization. *C. M. Wenyon.*

BERBERIAN, D. A. **Cutaneous Leishmaniasis (Oriental Sore). IV. Vaccination against Oriental Sore with Suspensions of Killed** *Leishmania tropica. Arch. Dermat. & Syph.* 1944, Oct., v. 50, No. 4, 234–6. [Refs. in footnotes.]

The author, who has done a considerable amount of work on the subject of immunity in oriental sore, has shown that sores may be induced, for the purpose of producing immunity, by the intracutaneous inoculation of suspensions (in isotonic saline solutions) of the flagellate form of *Leishmania tropica*. As in the naturally acquired disease, immunity does not develop till the sores are commencing to heal but, as has long been known, the immunity when acquired is permanent. The author has also attempted to produce immunity in two volunteers by the inoculation of flagellates which had been killed by suspending them in 0·5 per cent. phenol in saline. The results were entirely negative, but in view of the successes reported by PESSOA and PESTANA [this *Bulletin*, 1942, v. 39, 674] in S. America the author is led to record his experiments here. Of the 32 volunteers, 9 received one, 8 two, and 15 three injections of the killed vaccine. At intervals varying from 31 to 367 days after vaccination, the volunteers, together with unvaccinated controls and others who had recovered from oriental sore, were inoculated with suspensions of living flagellates. The only persons who did not acquire oriental sore were those who had recovered. It is thus clear that the vaccination with killed flagellates did not produce any immunity. The author finds it difficult to account for the successes reported in S. America where, however, no attempt was made to test the immunity of vaccinated persons by experimental inoculations. He considers the four-month period of observation too short. It should have been extended to a number of years. It seems clear that the S. American work needs confirmation.

C. M. Wenyon.

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KATZENELLENBOGEN, I. **Vaccination against Oriental Sore. Report of Results of Five Hundred and Fifty-Five Inoculations.** *Arch. Dermat. & Syph.* 1944, Oct., v. 50, No. 4, 239–42, 1 fig.

At the Palestine Potash Plant at the northern end of the Dead Sea, where oriental sore has become hyperendemic, the author vaccinated 556 persons with living leishmania from cultures or the spleens of infected hamsters. It was possible to follow up 416 of these and it was found that a vaccination sore developed in 237 after an incubation period varying from less than a fortnight to 18 months. Of those vaccinated, 11 were children, the youngest being three months old. The course in children was the same as in adults, except in one case where, as a result of trauma, there developed a slow-healing flat ulceration of the size of the child's palm and resembling scrofuloderma. Healing occurred in three months. When a sore is developing there appears at the end of the incubation a bluish red papule which persists for three to six months. The papules are easily injured, and may thus be converted into ulcers. There does not seem to be any reason to record the sores as nodules or ulcers.

In 45 cases a reaction occurred after vaccination. There was swelling at the site of injection, sometimes with infiltration of an area the size of a palm. Temperature up to 103°F. might be noted, with local pain and tenderness of the inguinal lymph nodes. The condition lasted not more than one to three days. In only four of these 45 did a vaccination sore develop. It would seem that the reaction was allergic in nature, for 26 of the subjects had resided in the area for several years. Such reactions are known to follow vaccination in persons previously infected with leishmania. On the other hand 27 persons who had been living in the area for several years and who showed no obvious signs of healed sores failed to develop sores on vaccination. Seven of these were vaccinated on two subsequent occasions, also without result. In these the possibility of a natural immunity has to be considered.

Persons inoculated six to eight months after the appearance of natural sores may develop, at the site of inoculation, nodules which contain no leishmania and which disappear within a few days or a week. Such reaction nodules may follow the inoculation of persons who have been suffering from relapsing oriental sore of several years' duration. The author's campaign of vaccination has had very favourable results. Thus, at one settlement during the last two years there have been 95 new arrivals. Of these 25 were vaccinated on the thigh. Not one acquired a natural infection, but of the 70 who were not vaccinated 65 became infected. *C. M. Wenyon.*

BELTRÁN, E. Acción de los cambios de pH sobre *Leishmania brasiliensis* en cultivo, y sus contaminaciones bacterianas. [**Effect of Changes of *p*H of *L. brasiliensis* Cultures and their Bacterial Contaminations.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1944, June, v. 5, No. 2, 97–100. English summary.

It occurred to the author, who had cultivated *Leishmania brasiliensis* in N.N.N. medium with a *p*H of 7·2, that it night be possible to find a *p*H which would be favourable to the growth of leishmania and at the same time prohibit the growth of bacteria liable to contaminate the cultures. After trial of various *p*H under 7·2 it was found impossible to exclude bacterial growth without at the same time excluding the leishmania. *C. M. Wenyon.*

FEVERS OF THE TYPHUS GROUP.

GEAR, J. **The Rickettsial Diseases in South Africa with special reference to Louse-borne Typhus Fever.** *Proc. Transvaal Mine Med. Officers' Ass.* 1944, Aug., v. 24, No. 265, 23–34, 3 charts. Discussion 34–7.

The following points of general interest are taken from this concise and vivid account of louse-borne typhus in South Africa.

The classification of the typhus fevers proposed by FELIX [this *Bulletin*, 1943, v. 40, 230], and based on the agglutination responses, has the advantage that these reactions can usually be determined, but in many cases they do not indicate the vector concerned, and this, from the point of view of the Health Officer, is the most important consideration. The classification proposed by MEGAW [this *Bulletin*, 1931, v. 28, 623] based on the vector, has the disadvantage that in any one case the vector is very rarely seen ; but a consideration of the attendant circumstances usually, though not always, gives a clear clue to its identity, and at present this classification into louse typhus, flea typhus, tick typhus, and mite typhus, is considered to be the most valuable.

In South Africa mite typhus is unknown, the other three types are of widespread occurrence.

The differentiation of louse typhus from flea typhus on epidemiological grounds is often difficult because of the frequent coexistence of infestation by lice and rats. Tick typhus is usually easy to diagnose in South Africa ; in most cases it is acquired by persons picnicking or camping in rural areas, though sometimes infection is associated with the presence of tick-infested dogs in the homes. There is usually a characteristic local lesion ; the rash is papular, and when profuse, it extends to the face, palms, and soles.

The Weil-Felix test, although non-specific, is one of the most reliable of the laboratory methods of diagnosis ; it does not differentiate louse typhus from murine typhus, and sometimes does not differentiate these from tick typhus. In tick typhus *Proteus OX19* and *OX2* are agglutinated, on the average, at about equal titres, and *OXK* is often agglutinated, as a rule at a lower titre. In most cases the agglutinins appear later than in louse-typhus—about the 10th day. When *OX2* alone is agglutinated the case is almost certainly one of tick-borne typhus.

A more specific reaction is the one based on the agglutination of the causal rickettsiae, but even this sometimes fails to differentiate louse typhus from flea typhus ; it usually gives a clear-cut differentiation of tick typhus.

A monocytosis of 7–15 per cent. is a constant and characteristic feature of typhus fever. Although flea typhus is widespread in South Africa, relatively few cases have been reported. Contrary to previous reports the Weil-Felix titres in louse typhus in South Africa are just as high as in Europe : in three consecutive cases the titres were ; 1–1,000 ; 1–2,800 ; and 1–25,000.

John W. D. Megaw.

GREIFF, D., PINKERTON, H. & MORAGUES, V. **Effect of Enzyme Inhibitors and Activators on the Multiplication of Typhus Rickettsiae. I. Penicillin, Para-Aminobenzoic Acid, Sodium Fluoride, and Vitamins of the B Group.** *J. Exper. Med.* 1944, Dec. 1, v. 80, No. 6, 561–74, 1 fig. [14 refs.]

The effects of penicillin, para-aminobenzoic acid (PABA), sodium fluoride, and vitamins of the B group, on the growth of murine rickettsiae in yolk-sac cultures were tested by the authors. The ingenious technique adopted will be of interest to other workers on the same lines.

The authors have already reported the action of penicillin in inhibiting rickettsial growth in yolk-sac cultures, and the beneficial effect of the drug

when given early to mice infected with typhus fever [this *Bulletin*, 1944, v. 41, 839 and 840]. UNGAR (*Nature*, 1943, v. 152, 245) [*Bulletin of War Med.*, 1944, v. 4, 301] has reported that PABA enhances the bacteriostatic effect of penicillin on some microorganisms.

In the present experiments the authors found that PABA, injected in doses of 3·3 mgm. into infected yolk sacs, had an inhibiting effect equal to that of 1,000 units of penicillin. Meta-aminobenzoic acid and ortho-aminobenzoic acid had no demonstrable effect.

PABA was added to the food of 23 " dba " mice infected with murine typhus. [The "dba" (dilute brown) strain of mice has been developed from a single pair by Dr. C. C. LITTLE, and has been inbred, for the most part, by brother to sister matings since 1909.] The drug was given from the first day after inoculation and in a strength of 3·0 per cent. Only one of the mice died of typhus, another died of some other disease on the 4th day. All the 23 untreated control mice which had been infected in the same way died o typhus fever on the 6th or 7th day.

Sodium fluoride accelerated the rate of growth of the rickettsiae in yolk-sac cultures. Various vitamins of the B group had no effect on the growth of the rickettsiae.

The favourable therapeutic effects of para-aminobenzoic acid in human typhus fever [this *Bulletin*, 1945, v. 42, 201] reported by YEOMANS *et al.*, were not known by the authors when they were engaged on the present experiments.

John W. D. Megaw.

NELSON, J. H. & CRUICKSHANK, J. C. **Agglutinins to Proteus OX19 in the Serum of Pregnant Women.** *Monthly Bull. Ministry of Health & Emergency Pub. Health Lab. Service (directed by Med. Res. Council).* 1945, Jan. v. 4, 19–25, 1 chart.

The authors have not been able to confirm the finding reported by GRATCH that the sera of pregnant women agglutinate *Proteus OX19*, constantly and at high titres [this *Bulletin*, 1944, v. 41, 197]. They have found that when an Oxford Standard Suspension of *Proteus OX19* was used, 6–10 per cent. of the sera of pregnant women agglutinated the organism at a titre of 1–100 or over. The two authors worked independently of each other and the following table shows their findings :—

Number of sera	Percentage agglutinating *Pr.OX19* at or over these titres (Ipswich series, by J.H.N.)				
	1–20	1–40	1–80	1–160	1–320
Normal sera 33 ...	39·4	24·2	12·1	3·0	0
Pregnancy sera 132 ...	87·1	62·1	33·4	10·6	0·8
	(Exeter series, by J.C.C.)				
	1–16	1–32	1–64	1–128	1–256
Normal sera 20 ...	35	20	5	0	0
Pregnancy sera 50 ...	88	64	32	6	2

In the Ipswich series an attempt was made to determine the stage of pregnancy at which agglutination responses were most frequent. No special trend could be detected, but among 50 sera taken during the 5th and 6th months 76 per cent. reacted at 1–40, 44 per cent. at 1–80, and 16 per cent. at 1–160.

Other organisms were found to be agglutinated more frequently by the sera of pregnant women than by normal sera ; CRUICKSHANK found the following

percentages of reactions at titres of 1–80 or over among 45 pregnant women : *Proteus OX2*, 8·3 ; *Bact. typhosum O*, 4·4 ; *Bact. paratyphosum BO*, 13·3. Sera of 27 pregnant women did not agglutinate suspensions of epidemic and murine rickettsiae although the sera used had already agglutinated *Pr. OX19* at titres of 1–40 or over.

The authors state that in the absence of more detailed information concerning technique they are unable to explain the difference between their findings and those of Gratch. They suggest that he may have used a hypersensitive strain and they point out that no mention is made of the use of a standardized suspension. They do not exclude the possibility that Gratch's strain possessed some distinctive character, but they conclude that the test is not likely to have any application in the early diagnosis of pregnancy.

[The difference in the findings seems to be best explained by the existence of a " distinctive character " in Gratch's strain. A happy event of this kind would not be unprecedented, because, according to Felix, *Proteus OXK* is an antigenic variant of *Pr. OX19*, being derived from a culture of that organism supplied by the National Collection of Type Cultures. It is to be hoped that the " Gratch strain " is still available and that subcultures will be found to be as " specific " for the sera of pregnant women as *Pr.OXK* is for the sera of mite-typhus patients.] *John W. D. Megaw.*

Varela, G. Presencia en el cobayo normal de un antigeno que origina la reaccion de Weil-Felix. [**The Presence in the Normal Guineapig of an Antigen which gives rise to the Weil-Felix Reaction.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1944, Sept., v. 5, No. 3, 191–3. English summary (4 lines).

Suspensions prepared by triturating the lungs of healthy guineapigs in normal saline were injected intravenously on six occasions into each of two healthy goats whose sera had been found to contain no agglutinins for *Proteus X19* or *Pr. XK*. A week after the last of these injections the sera of the goats agglutinated both of the above organisms at a titre of 1–160. By absorption and precipitin tests the agglutinins in the goats' sera were found to behave in the same way as those contained in the sera of typhus patients.

The author believes that " the absence of the Weil-Felix reaction in typhus-infected guineapigs is due to the presence of this antigen." He considers that the antigen which the guineapig possesses in common with the *Proteus* organisms is contained in the endothelial cells of the animal, and that this distribution accounts for the fact that the lung is specially rich in the antigen.

John W. D. Megaw.

Stevens, R. S. **Louse-borne Typhus Fever. Trial of Serum Treatment.** *Lancet.* 1945, Jan. 27, 106–9, 10 charts.

Hyperimmune rabbit serum made by the Lederle Laboratories was tried by the author in the treatment of seven cases of louse-borne typhus at a hospital in the Middle East. In the first case doses of 40 cc. were given intravenously on the 6th and 7th days, but the patient died on the 9th day ; he belonged to the 36–39 age group. In the other six cases the treatment was started as soon as the diagnosis was made ; the dosage was : 40 cc. intravenously, and 40 cc. intramuscularly, on the first day of treatment ; 40 cc. intramuscularly on the next day ; and 20 cc. by the same route on the following days till necessity for the treatment was no longer apparent. All these patients survived, and there were grounds for believing that their condition had been improved by the injection of serum, though the author states that " no attempt is made to draw conclusions from so small a series."

Among 14 patients who had been treated in the hospital before the serum became available there were five deaths. Brief notes are given of the 21 cases. It is mentioned that the average delay in appearance of a Weil-Felix titre of 1–100 was 11·6 days. Two patients who died had completely negative reactions on the 8th day, and in another fatal case the titre was 1–40 on the 7th and 11th days. Rickettsiae were isolated from two of these three patients. Rickettsia-agglutination reactions were positive at high titres in the six cases in which the test was carried out. *John W. D. Megaw.*

LAMPERT, H. Eine neue Allgemeinbehandlung schwerer Infektionskrankheiten, erläutert am Fleckfieber. [**A New General Method of Treatment of Severe Infectious Diseases, as Applied to Typhus Fever.**] *Münch. med. Woch.* 1944, May 5, v. 91, No. 17/18, 223–5.

The author has already claimed that he has obtained excellent results in the treatment of typhus fever, by the daily use of warm baths, daily intravenous injections of artificial blood, and repeated subcutaneous or intravenous injections of saline solutions [see this *Bulletin*, 1942, v. 39, 824, and 1943, v. 40, 831]. Further evidence in support of this claim is now produced, but as was the case in connexion with the previous papers it is not easy to assess the significance of the results that have been reported.

In the first set of figures the controls consisted of patients in a neighbouring hospital. In January and February 1942, there were no deaths among 104 patients treated at the author's hospital, and at the other hospital the fatality rate was 13·3 per cent. In the following two months 11 per cent. of the author's patients died, and 14·4 per cent. of the controls.

The physician whose patients served as controls in the above series later applied the hot-bath treatment to 96 of his patients and 10 of these died, whereas the fatality rate for all the 323 patients treated at the hospital during the same period was 13 per cent. No mention is made of the manner in which the 96 patients were selected for the treatment.

In November 1942, alternate patients were admitted to each of two hospitals of 100 beds; at one of these the combined treatment was carried out and the fatality rate was 6·7 per cent. among 178 patients; at the other hospital no baths were given and intravenous injections were administered only in special conditions; the fatality rate in 185 patients was 17·8 per cent.

The author claims that his system of treatment has been demonstrated to be strikingly effective and he holds that it would be equally suitable for all severe infectious diseases.

The only information regarding the hot-bath technique is contained in the statement that the bath at first ought to be at the same temperature as the patient and should be warmed gradually.

[It does not appear that the treatment has been adopted by other German physicians to the extent that would be expected if results comparable with those mentioned in the last of the above trials could be obtained by other observers.] *John W. D. Megaw.*

SERGENT, E. & HORRENBERGER, R. Utilisation de la chèvre pour la préparation du vaccin non vivant contre le typhus exanthématique avec du virus provenant de pneumonie rickettsienne provoquée [**The Use of the Goat for the Preparation of Killed Typhus Vaccine.**] *Arch. Inst. Pasteur d'Algérie.* 1944, Mar., v. 22, No. 1, 8–10.

The authors trace the history of the discovery by CASTAÑEDA [this *Bulletin*, 1940, v. 37, 261] and by DURAND and SPARROW [*ibid.*, 1940, v. 37, 572] (independently) that the lungs of mice, infected intranasally with rickettsiae,

formed an excellent source of vaccine. Formalin vaccines prepared in North Africa were found to be effective, and later the use of rabbit lung preparations was adopted, by means of which the yield of vaccine was greatly increased. COMBIESCU *et al.* [*ibid.*, 1943, v. 40, 34] experimented with dogs, but the yield was poorer in rickettsiae than that from mice, but HORRENBERGER and RENOUX [*ibid.*, 1945, v. 42, 107] in Algiers found that sheep gave good results. It is now known that the yield from goats is as good as that from mice, and the goat offers certain advantages over the other animals; it can be infected from the mouse.

The authors refer briefly to the protection given to those who work in the typhus laboratories:—vaccination and regular re-vaccination, the use of protective clothing and masks, supplementary rations, adequate holidays and rest. In two years only three of 30 persons have contracted typhus, which was slight. This, by the standards in other laboratories, is a low figure.

Charles Wilcocks.

GIROUD, P. Le tissu pulmonaire privé de Rickettsies par lavage et centrifugation possède un pouvoir antigène certain. [**Pulmonary Tissue deprived of Rickettsiae by Washing and Centrifugation possess Antigenic Properties.**] *C. R. Soc. Biol.* 1943, May, v. 137, No. 9/10, 271–2.

The lung tissues of infected mice and rabbits were washed and centrifuged 13 times so as to separate, as far as possible, the rickettsiae from the tissues. Rickettsiae could not be demonstrated in smears from this tissue, but by enrichment methods the presence of small numbers could be confirmed. Vaccines were prepared in formol saline from the tissues thus largely (but not completely) deprived of the organisms, and were used for immunization tests, control animals being inoculated with the same vaccine, but with the addition of the rickettsial suspension which resulted from the centrifugations.

The tissue vaccine gave protection similar to that afforded by the mixed vaccine, to animals subsequently inoculated with a highly virulent strain of North African typhus. Lung tissue, therefore, in which there has been abundant growth of rickettsiae, possesses good antigenic properties. *Charles Wilcocks.*

GIROUD, P. Pouvoir pathogène et antigène sur cobaye de doses massives de Rickettsies du typhus historique, conservées à −25° pendant des temps très longs. [**Pathogenic and Antigenic Power of Massive Doses of *Rickettsia prowazeki* preserved at −25°C. for Long Periods.**] *C. R. Soc. Biol.* 1943, May, v. 137, No. 9/10, 273–4.

Infected animal lungs were kept for 5 to 39 months at −25°C. in unsealed tubes; the tissues gradually dried. Doses corresponding to one-half or the whole of one lung were injected intraperitoneally into guineapigs at various times. The results were rather irregular, but infection took place even with material preserved for more than 14 months.

Only those animals were found to be immune which had showed febrile evidence of infection. The author concludes, therefore, that the infective and antigenic powers of the rickettsiae are lost at the same time; it is improbable that attenuation with preservation of antigenicity can be achieved by these means. *Charles Wilcocks.*

RUIZ MORENO, F. Caso de tifo exantematico en Baja California. [**A Case of Typhus in Lower California.**] *Medicina.* Mexico. 1944, Dec. 25, v. 24, No. 474, 471–2.

SIEDEK, H. Zur Kreislaufpathologie des Fleckfiebers. [**The Pathology of the Circulatory System in Typhus.**] *Wien. klin. Woch.* 1944, June 16, v. 57, No. 23/24, 298–301.

COOK, C. E. **Observations on the Epidemiology of Scrub Typhus.** *Med. J. Australia.* 1944, Nov. 18, v. 2, No. 21, 539–43. [12 refs.]

Three outbreaks of scrub typhus are discussed from the point of view of epidemiology.

Outbreak A consisted of 45 cases which occurred within a period of four weeks. Infection was confined to soldiers who had entered a strictly limited locality on the bank of a creek close to the edge of a jungle area. Although three divisions had been operating in the surrounding area of thickly wooded country, and although scrub itch due to the bites of mites was very prevalent in the whole region, no other cases of scrub typhus occurred.

Outbreak B also affected persons camping close to a creek in open forest country. There were 37 cases within a period of three weeks. No scrub itch occurred, and " mite surveys were unproductive."

Outbreak C. In two brigade groups there were some hundreds of cases, all from units camped near jungle fringes on the banks of streams. Units in the open valley for the most part escaped scrub typhus.

Infection was intense in very restricted foci limited to areas on the banks of jungle-clad streams, and there was evidence that infection persisted year after year in certain foci. The incubation period ranged from 10 to 21 days.

A study of these outbreaks and of the available evidence on the subject of transmission led the author to doubt whether mites were really the vectors, and he argues at some length that larval ticks are more likely to be responsible for transmitting the disease.

[This view is likely to give rise to sharp controversy so it is considered better to postpone a review of the arguments brought forward till the other side of the case has been stated.]

The author's view, in brief, is that there is no evidence to incriminate any one particular species of mite, and that the epidemiology of the disease is consistent with its transmission by larval ticks.

[In the meantime preventive measures directed against bites by mites will be equally effective against tick bite, and both of these arthropods must always be regarded as potential menaces to the efficiency of armies in the East.]

John W. D. Megaw.

[The suggestions that scrub typhus may be transmitted by ticks has been made before by investigators in the Netherlands East Indies, see KOUWENAAR and WOLFF, this *Bulletin*, 1936, v. 33, 442, and VAN DER SCHROEFF, *ibid.*, 1941, v. 38, 684.—*Ed.*]

WILLIAMS, R. W. **A Check List of the Mite Vectors and Animal Reservoirs of Tsutsugamushi Disease.** *Amer. J. Trop. Med.* 1944, Nov., v. 24, No. 6, 355–7. [20 refs.]

The geographical distribution, mite vectors, and animal reservoirs of mite-borne typhus are shown in Table I. The author refers to the report of VAN DER SCHROEFF [this *Bulletin*, 1941, v. 43, 684] on typhus in Northern Sumatra, where ticks (*Amblyomma*) were possible vectors as well as mites, and to a report by the U.S. American Typhus Commission [*ibid.*, 1944, v. 41, 841] on typhus in New Guinea, where " scrub itch " and " scrub typhus " showed little correlation.

TABLE 1.

Mite vectors and reservoir animals of Tsutsugamushi disease

Geographical Distribution	Mite Vector	Reservoir
Australia ...	*Trombicula deliensis* Walsh, 1923 (1) *T. minor* (*hirsti* Sambon, 1927) (1) †*Laelaps australiensis* (2)	**Isoodon torosus* – Bandicoot (1) **Melomys littoralis* – Rat (1) **Rattus assimilis* – Rat **Rattus conatus* **Rattus norvegicus* (white strain) (1) **Rattus norvegicus* (black and white strain) (1) **Rattus rattus* (1)
China	*T. akamushi* Brumpt, 1910 (3)	?
Formosa ...	*T. akamushi* (3, 4)	*Rattus rattus rufuscens* (3, 9) *Rattus rattus rattus* (5) **Rattus losea* (5, 11) *Rattus* (*Apodemus*) *agrarius* (5, 3) *Rattus norvegicus* (3) *Rattus musculus* (3) *Pachyura murina* – Musk Shrew (3)
India	*T. deliensis* (6) *T. acuscutellaris* Walsh, 1923 (6)	*Mus* (*Rattus*) *rattus* (6) *Mus decumanus* *Mus bactrianus* (6) *Golunda ellioti* – Indian brush rat (6) *Nesocia begalensis* – Mole rat (6)
Japan	*T. akamushi* (4, 7, 9)	**Microtus montebelloi* Vole–(4, 7, 9) *Arvicola hatanedzumi* – Field mouse (8)
Malaya	*T. akamushi* (4) *T. deliensis* (9) ‡*Schöngastia shüffneri* Walsh, 1923 (9)	*Mus rattus* (4) *Mus concolor* (4)
New Guinea ...	§*T. minor* (10) *T. deliensis* (1)	*Echymipera cockerelli* – Bandicoot (10)
Pescadores Is. ...	*T. akamushi* (11)	**Mus rattus rufescens* (11)
Sumatra ...	*T. akamushi* (12) *T. deliensis* (9, 3) *S. shüffneri* (9, 3)	*Rattus rattus diardii* (9, 3) *Mus concolor* (3)

* Animals in which the rickettsial organism has been demonstrated in nature, and which act as hosts of the mite vectors.

† Not a chigger mite.

‡ Thought to transmit the disease only from man to man. Belongs to genus indicated rather than Neoschöngastia as placed by some authors.

§ Some authors have placed the New Guinea form of this mite in the genus Neoschöngastia.

J. F. Corson.

McCULLOCH, R. N. **Notes on the Habits and Distribution of Trombiculid Mites in Queensland and New Guinea.** *Med. J. Australia.* 1944, Nov. 18, v. 2, No. 21, 543–5.

Medical entomologists must read this paper in its complete form, but a few points of special interest to medical men in the East are given in the following abstract.

The six-legged larval mites which attack man have much the same feeding habits as ticks ; they remain attached till fully engorged ; in some species this process takes as long as two days. Mites that are seeking a blood meal can safely be collected by a person whose clothes are impregnated with one of the suitable insecticides. The mites are picked up with a camel-hair brush, moistened with alcohol, as they travel across the boots of the collector ; who must stand quite still.

In West Queensland, scrub itch is caused by *Trombicula minor*, which may be exceedingly plentiful.

Mites are most active on warm days (67–75°F.) and are inactive at temperatures below 60°F. They are not felt as they crawl over the skin, or when biting, or for 10–18 hours after attaching themselves. Then itching begins and the mites can be found in the centre of small raised and reddened areas of skin of about one-quarter inch in diameter.

In New Guinea the ankles were more heavily attacked than the trunk, but on the Atherton Tableland in North Queensland the bites were on the parts of the body covered by clothing, and not specially on the ankles.

It is suggested that the mites are attracted by sweat and so tend to travel till they reach a part of the body that is bathed in sweat.

There is no certain knowledge of the species of mites that are responsible for transmitting scrub typhus ; all of them must be suspected.

The author does not accept the suggestion that there is a special " typhus mite " which does not cause itch and which prefers to attack the trunk rather than the legs. He often found it quite impossible to predict that a given area of ground would be infested ; sometimes the mites are most numerous on grassy hills, sometimes in the jungle. They are much more active after rain than during rain or in dry weather. They rarely climb higher than three inches up the stems of grass or bushes. Persons walking in infested areas are not likely to be bitten ; but standing still, sitting, or lying down, whether by day or by night, are direct invitations to the mites.

Cutting and burning the grass of camp sites reduces the number of the mites but does not eliminate them. Paths, trampled ground, and the floors of tents or buildings, soon become free from mites. *John W. D. Megaw.*

WILLIAMS, S. W., SINCLAIR, A. J. M. & JACKSON, A. V. **Mite-borne (Scrub) Typhus in Papua and the Mandated Territory of New Guinea : Report of 626 Cases.** *Med. J. Australia.* 1944, Nov. 18, v. 2, No. 21, 525–39, 11 figs. (1 on coloured pl.).

This detailed account of the clinical features of scrub typhus is based on experience of 626 cases treated at an Australian general hospital in New Guinea between September 1942 and the end of September 1943. More than half of the infections were contracted during the fighting on the Moresby-Buna trail ; 97 occurred during the campaign in and round Wau.

In most respects the description of the signs and symptoms corresponds closely with one of louse-borne typhus, but some of the special features deserve attention.

By the end of the second week, *Proteus OXK* was agglutinated at a significant titre in most of the cases. After attacks of average severity the patients became

fit for duty at the end of 12 weeks ; after mild attacks this period was reduced to 6–8 weeks. Ambulatory attacks also occurred in which the only evidence of illness was the agglutination response.

There was some difficulty in getting a satisfactory strain of *OXK*, but when this was secured, it was subcultured without loss of its agglutinability over a period of 12 months.

The rise in titre began between the 8th and 13th days ; the maximum was reached between the 14th and 22nd days. A significant titre was regarded as one showing a " two-tube increase " ; for example from 1–25 to 1–125 or from 1–50 to 1–250. When patients were seen for the first time late in the illness, a titre of 1–125 was regarded as significant. Among 2,000 control sera, only one false positive was detected.

In 8 per cent. of undoubted cases the titre did not exceed 1–25, and in an additional 6 per cent. it was 1–50. Among fatal cases negative or non-significant reactions occurred in 25 per cent. of the patients, though very high titres were observed in some.

A simple slide test was tried in 300 cases. One drop of serum previously diluted 1–4 was mixed on a slide with a drop of concentrated *OXK* suspension, and the reading was made after rocking the slide for 2–3 minutes. The method was quite satisfactory with sera giving reactions of 1–500 or over with the standard method, but sera of lower agglutinability gave irregular reactions.

An analysis was made of the duration of the fever in 508 cases ; it was 4–8 days in 12 ; and 26–40 days in 15. The usual duration was 12–20 days ; in 276 cases it ranged between 14 and 18 days.

An eschar was seen in 59 per cent. of the cases ; the patients seldom knew of its existence or of the bite that presumably was its cause. At the onset of the fever it was a rounded sore, 2–3 mm. in diameter, surrounded by a dusky-red raised areola, 3–4 mm. in width.

The necrotic centre had sloughed out by the 10th to the 20th day leaving a punched-out ulcer surrounded by a bright-red areola. In rare cases, there were two or more eschars ; in one case there were six. The site was seldom distal to the knee or elbow ; none occurred on the hand or foot.

A rash was seen in 65 per cent. of the cases ; it usually appeared between the fifth and eighth days ; at first there were reddish macules, about 2–5 mm. in diameter, on the chest and the front of the abdomen, soon the spots became maculo-papular, the rash extended to the face and limbs, including the palms and soles, and the spots became larger.

Generalized enlargement of the lymph glands was observed in 66 per cent. of the cases : it was pronounced by the fourth or fifth day, and was usually greater in the glands draining the area of the eschar.

The leucocyte count was very variable ; during the first ten days the total count ranged from 3,100 to 12,400 per cmm., and during the second ten-day period it was 3,100–20,000 per cmm. The only significant change was in the lymphocytes, whose numbers rose steadily in all the cases in which there was a good reaction to the infection, so that by the 8th to the 15th day counts of 3,000 were usual. In fatal attacks this increase in the lymphocyte count was exceptional.

The total fatality rate was 9·7 per cent., but there were remarkable variations: among the first 100 patients there was only one death ; among the second 100 there were two ; in the next 150 there were 37 (25 per cent.). The excessive mortality rate in the last-mentioned group was due to lowered resistance caused by great hardship, dysentery, and malaria. In the later period the fatality rate was 7·2 per cent.

The treatment was on the lines suitable for louse-borne typhus ; the patients were nursed, when possible, in the Fowler position ; a fluid intake of at least

140 oz. daily was aimed at ; the diet was well supplied with carbohydrates and proteins. Blood transfusion was very seldom needed, except for a few cases of anaemia which occurred during convalescence. Cardiac stimulants were found to be of very little value. There was no evidence of permanent cardiac disability.

A typical eschar is well shown in a coloured photograph in the paper.

[This article is of exceptional value and importance at the present time ; it must be consulted by everyone who undertakes the work of describing the clinical aspects of mite-borne typhus as a war disease.] *John W. D. Megaw.*

McDonald, S. F. **Scrub Typhus.** [Correspondence.] *Med. J. Australia.* 1944, Dec. 2, v. 2, No. 23, 601.

The author, as a consultant and repatriation doctor, calls attention to two points which he thinks were not emphasized sufficiently in the paper on mite-borne typhus by Williams, Sinclair and Jackson [above] ; they relate to the heart manifestations and the paralyses. Mite typhus, as Williams *et al.* stated, leaves no permanent cardiac damage, but a belief is common among both medical men and soldiers that any extra exertion during convalescence may cause sudden fatal heart failure. Such a view is very likely to produce many cases of D.A.H. The paralysis of the limbs also seems to clear up completely, but sometimes it continues as a purely hysterical condition ; if it persists for more than a few weeks, the muscles should be tested with the faradic current. *J. F. Corson.*

Lipman, B. L., Casey, A. V., Byron, R. A. & Evans, E. C. **Scrub Typhus. Results of a Study of the Cases of Two Hundred Patients admitted to and treated at a Station Hospital between Feb. 9, 1943 and Feb. 4, 1944.** *War Medicine*, Chicago. 1944, Nov., v. 6, No. 5, 304–15, 4 charts

This informative paper deals with the clinical features of scrub typhus, of which 200 cases were seen by the authors at a hospital in North New Guinea between February 9th, 1943 and February 4th, 1944.

The patients were engaged in military operations in coastal and foothill areas.

A detailed account is given of the post-mortem changes observed in six cases, but in five of these lobar pneumonia had occurred as a complication, so that, as usually happens in the typhus fevers, the picture was somewhat confused. The lesions uniformly present were the eschar, lymphadenopathy, the rash and enlargement of the spleen. In three cases the vessels of the pia mater were moderately injected. Small haemorrhages, under the pleura, in the pericardium, and in the gastro-intestinal mucosa, were seen in two cases. The microscopic changes characteristic of the disease were the " typhus nodules," which were most conspicuous in the smaller vessels of the heart, lungs and brain.

The incubation period was 9–14 days ; the eschar, which was detected in 80 per cent. of the cases, was usually formed during this period ; its presence had seldom been detected by the patient, it was located on the extremities and trunk, usually below the umbilicus. Regional or generalized lymphadenitis occurred in 98 per cent. of the cases ; the femoral and inguinal glands were most often affected.

The prodromal period lasted 1–5 days and the chief features during this stage were malaise, headache, backache, pains in the orbital region, and swollen and tender glands in the region draining the site of the eschar. The temperature was 99·6–102°F. towards the end of the prodromal period. The onset was usually gradual, though sometimes it was acute. The febrile period lasted 14–18 days and ended by lysis. The most usual temperature was 101°F. in the morning, and 104° in the evening. The rash was seen in 85 per cent. of the

cases ; it appeared between the fifth and eighth days, on the front and sides of the chest and abdomen, and was maculo-papular ; the extremities were less affected than the trunk, and though it occasionally extended to the face it was less frequent there than was a general flush accompanied by injection of the conjunctivae.

In severe attacks euphoria was frequent at an early stage ; later there were muscular twitchings, stiffness of the neck, delirium, mania, or even coma. Deafness lasting 2–3 weeks, was not uncommon.

The complications, in approximate percentages, were: pulmonary congestion, 50 ; infectious myocarditis, 45 ; suppurative bronchitis, 20 ; bronchopneumonia, 9 ; pleural effusion, peripheral neuritis, and thrombophlebitis, 5 each ; lobar pneumonia, 4 ; pulmonary emboli, and splenic infarction, 2·5 each. [The name " infectious myocarditis " used in the above list of complications seems to be misleading; from the text it appears that the cardiovascular complications are attributed to three different causes, damage to the myocardium, damage to the peripheral blood vessels, and damage to the vasomotor centres. The authors state that " Peripheral vascular failure may occur independently of, or associated with, congestive heart failure. It is our opinion that complicating peripheral failure is of central or peripheral origin and is due to a specific action of the concerned toxin on the vasomoter centre or the peripheral vascular bed." They also state that " cardiovascular complications " occurred in 20 per cent. of the first 101 cases and 70 per cent. of last 99 cases, so that presumably the term infectious myocarditis is used without prejudice to the exact classification of the condition.]

Leucocytosis occurred only when there were complications, otherwise there was leucopenia or a normal count. The sedimentation rate was increased to a varying degree, its only significence seems to be that a slow return to normal progressed *pari passu* with the patient's restoration to health, so that the test might be useful as an index of recovery.

In the first 100 cases *Proteus OXK* was agglutinated at high titres ; in the second 100 the titres were much lower so that a rise of titre from 0 to 1–40 came to be regarded as diagnostic. The authors suggest that the change was due to " a variation in the antigen." They also state that positive reactions occurred " as early as the ninth day and as late as the 36th."

Lumbar puncture was done in six cases, because of severe cerebral manifestations ; in three of these the fluid was found to be at high pressure (200 to 260 mm. water) ; and by withdrawing about 30 cc. of fluid the pressure was reduced to 120 and the symptoms were greatly relieved.

The fatality rate was 10 per cent. ; it was much higher than this among patients arriving from the combat zone and among those belonging to the higher age groups. Of 13 officer patients six died ; four of these were more than 35 years of age.

Convalescence was prolonged, " neurasthenia, weakness, dyspnoea, and tachycardia, persisted for 2–3 months on the average."

Treatment was largely symptomatic. Incipient peripheral vascular failure was treated by oxygen, vasomotor stimulants (peripheral or central), and blood plasma. For congestive heart failure, double-concentrated plasma, given by repeated small intravenous transfusions, and digitalization were used. Sulphadiazine or sulphathiazole had excellent effect in pneumonia ; the former failed in one case and penicillin was given intramuscularly in doses of 20,000 units every four hours to a total of one million units, with good result. Penicillin had no demonstrable effect in a case in which there were no complications. Convalescent serum was given intramuscularly to two patients early in the disease in daily doses of 25 cc. for five days ; there was no apparent benefit.

John W. D. Megaw.

HARRELL, G. T., VENNING, W. & WOLFF, W. A. **The Treatment of Rocky Mountain Spotted Fever with particular reference to Intravenous Fluids. A New Approach to Basic Supportive Therapy.** *J. Amer. Med. Ass.* 1944, Dec. 9, v. 126, No. 15, 929–34, 3 charts. [13 refs.]

The authors challenge the views of distinguished workers like TOPPING [*M. Clinic, N. America*, 1943, v. 27, 722, and this *Bulletin*, 1943, v. 40, 837] and PARKER, who have suggested that intravenous medication does more harm than good in Rocky Mountain spotted fever. They claim that excellent results are obtained when laboratory procedures are used to control the type and amount of the injections.

Three cases are described to show the methods employed. In one case transfusions of saline and glucose were given by the intravenous route daily for nine consecutive days in quantities ranging from 1,000 to 2,500 cc. in addition to the oral administration of 2,400 to 3,700 cc. of fluid. Plasma or blood was also given to this patient on five occasions in doses of 450 to 1,000 cc. by the vein. In this case the large intravenous doses of salines and glucose were thought to be causing oedema and deterioration of the patient's general condition, but when blood and plasma were given the oedema promptly disappeared.

From the details given in the charts of the elaborate tests that were repeatedly carried out it is obvious that the treatment was controlled in a manner that would be quite impracticable in ordinary hospitals or in field conditions.

The general claim is made that the collapse of the peripheral circulation which occurs in the disease corresponds to a condition of shock and that full doses of plasma or blood are needed. Saline and glucose solutions, when given alone, may do more harm than good because they tend to reduce the already depleted protein content of the blood.

The use of convalescent blood or plasma did not appear to have any advantages over normal blood fluids.

[This paper is of special interest at the present time because the general lines of treatment of Rocky Mountain spotted fever must correspond closely with those suitable for the other fevers of the typhus group.]

John W. D. Megaw.

YELLOW FEVER.

LINHARES, H. Substâncias antibióticas. Ação dos filtrados de cogumelos e bactérias sôbre o virus amarilico neurotrópico. [**Antibiotic Substances. The Actions of Filtrates of Moulds and Bacteria on Neurotropic Yellow Fever Virus.**] Reprinted from *Hospital*. Rio de Janeiro. 1944, Sept., 327–97, 8 charts. [394 refs.] English summary.

Filtrates of cultures of *Aspergillus flavus*, *Penicillium camemberti* and a species of *Actinomyces* were found to have a lethal effect upon the neurotropic strain of yellow fever virus, both *in vitro* and *in vivo*. When a virus suspension was mixed with filtrate and immediately inoculated into mice intraperitoneally (together with an intracerebral injection of starch) a high proportion (up to 80 per cent. in some cases) of animals survived. Similar results were obtained when the virus and filtrate were inoculated after standing in contact for one hour. Filtrate was also inoculated 2–4 hours before the virus, or 24 and 4 hours before and on the two following days. In both series of experiments similar protection was observed. The results are based upon the inoculation of over 6,000 mice; full controls were used, and the differences in death rates between experimental animals and controls were striking.

The virucidal principle first appeared in filtrates of seven-day-old cultures, and attained maximum concentration between the 7th and 12th day; this is

correlated by the author with the sporulation of the moulds which takes place at this time. The active principle was destroyed in 10 minutes at 115°C. or 100°C., but could withstand 75°C. for 30 minutes and 56°C. for one hour; it passed through a Seitz filter. A non-infective mixture of virus and filtrate possessed antigenic properties, so that mice inoculated with it were resistant to a test inoculation of active virus three weeks later.

Filtrates from cultures of certain bacteria were also tested; none showed any antiviral activity. *D. J. Bauer.*

KIRK, R. & BAYOUMI, A. **Notes on a Fatal Case of Yellow Fever.** *Ann. Trop. Med. & Parasit.* 1944, Dec. 30, v. 38, Nos. 3 & 4, 205–6.

A record of the first fatal European case of yellow fever observed in the Sudan. The patient, an Italian missionary, lived at Torit, Southern Sudan, and had not previously been immunized against the disease. He became ill in October 1942, and died at the beginning of the ninth day of illness. The clinical and pathological features were typical. Sections of the liver showed the characteristic histopathological changes and blood collected on the sixth day of illness protected mice against yellow fever virus in standard mouse protection tests.

The main interest of this record lies in the fact that although thousands of cases of yellow fever infection have been observed in Africans in the Sudan, hitherto only five European cases had been identified, which all ended in recovery, and three were so benign that they would not have been recognized without the use of immunological tests [see this *Bulletin*, 1942, v. 39, 69, 457]. The present case presented most of the classical signs and symptoms of fatal yellow fever described by the early observers in America and West Africa.

E. Hindle.

HENDERSON, C. A. **Control of *Aedes aegypti* in Savannah.** *Pub. Health Rep.* Wash. 1944, Oct. 13, v. 59, No. 41, 1350–52.

In 1943, *Aëdes aegypti* was found to be breeding on more than one-third of the premises in Savannah; this was a serious position, since it is known that breeding in 1 to 5 per cent. of premises is enough to permit an outbreak of yellow fever, and under the conditions of modern inter-continental travel, the disease may be introduced from South America. The Control Unit established in Savannah employs inspectors who have now thoroughly examined all premises and destroyed all potential or actual breeding places found, or induced the occupiers to do so. Publicity for the campaign was invoked through the press and radio, etc., and the result has been a general clean-up of garbage, debris and rubbish throughout the city. Thus the Unit, with 5–10 inspectors, has, with the co-operation of the public, shown that a control programme is feasible. In June 1944 less than 2 per cent. of premises were breeding *Aëdes aegypti*.

Charles Wilcocks.

DENGUE.

ELEK, S. R. **Altered Taste in Dengue.** *War Medicine*, Chicago. 1944, Dec., v. 6, No. 6, 392–4.

To 154 patients suffering from dengue in New Guinea the question was put: "Have you any odd or funny taste in the mouth?"; in 86 per cent. of the cases the reply was in the affirmative, 63 per cent. of those who noticed an odd taste described it as "bitter", 24 per cent. as "sour", 5 per cent. as "sweet", and 8 per cent. gave various other descriptions.

Only 29 per cent. of 76 malaria patients admitted to having noticed any change in the taste, and on the strength of this difference the author suggests that the

symptom may be useful in differentiating dengue from malaria. He also suggests that it may be helpful in the differential diagnosis of sandfly fever, because one observer is reported as stating that he had never observed the symptom in the latter disease [but presumably he had not put a leading question to his patients'].

In the outbreak of dengue dealt with in this note a rash was observed in 31 per cent. of the patients; a "saddle-back" temperature curve was not seen in any of the cases. *John W. D. Megaw.*

Steinhaus, E. A. & Parker, R. R. **The Isolation of a Filter-passing Agent from the Rabbit Tick *Haemaphysalis leporis-palustris* Packard.** *Pub. Health Rep.* Wash. 1944, Nov. 24, v. 59, No. 47, 1528–9.

In this brief and succinct report the authors describe a finding of exceptional interest.

Five lots of rabbit ticks, *Haemaphysalis leporis-palustris*, were collected in July 1943 at Camp Bullis in Texas. From each of two of the lots a strain of an unidentified filter-passing virus was isolated by combined subcutaneous and intradermal injection of pooled suspensions into guineapigs.

One of the strains was isolated from a lot consisting of 32 adult ticks and one nymph; the other was from a lot of 36 adults and 10 nymphs.

Mice and rabbits were susceptible to the virus, but guineapigs gave the most distinct reactions, and were susceptible to subcutaneous, intraperitoneal, and intracerebral injections, also to oral administration of infectious material.

After an incubation period of 4–10 days guineapigs had a febrile reaction lasting 2–6 days with temperatures of 39·6–40·4°C. No deaths occurred and the only consistent autopsy finding was enlargement of the spleen to 1½–3 times the normal size. The strains were maintained by consecutive passages through guineapigs, in one case up to 23 transfers. There was no cross immunity with Rocky Mountain spotted fever or American Q fever.

The virus was maintained in fertile hens' eggs for eight passages, killing 30–50 per cent. of the embryos. The agent in the eggs passed through Seitz and Berkefeld filters. No recognizable organism was found in smears made from infected animal tissues or eggs. All attempts to obtain cultures on artificial media of likely kinds failed.

The authors have maintained an attitude of scientific reserve in refraining from comment on the possible bearing of their finding on the aetiology of Bullis fever, of which 485 cases were reported during the two months preceding the one in which the ticks were collected from the same area. [See this *Bulletin*, 1944, v. 41, 34 and 666; 1945, v. 42, 205.]

The finding may also conceivably have a bearing on another tick-borne short fever—Colorado tick fever—which occurs not very far away, as distances go in the U.S.A., from Camp Bullis. [See this *Bulletin*, 1941, v. 38, 694; 1945, v. 42, 117, 118.] [The reviewer's speculative suggestion that a "zootic" tick-borne fever of the dengue group might occur in the Colorado and Texas areas become more plausible as a result of the present finding, though it still remains a speculation.] *John W. D. Megaw.*

PLAGUE.

Girard, G. Les ectoparasites de l'homme dans l'épidémiologie de la peste. [**The Rôle of Human Ectoparasites in Plague Epidemiology.**] *Bull. Soc. Path. Exot.* 1943, Jan. 13 & Feb. 10, v. 36, Nos. 1–2, 4–41, 1 fig. & 1 pl. [68 refs.]

This lengthy treatise deals primarily with the question of transmission of human plague in epidemic form by the flea of man, *Pulex irritans*, as sustained in argument by Blanc and Baltazard (*C. R. Acad. Sci.*, 1941, v. 213, 813 &

849) for Morocco. It is particularly valuable because, as the speakers who took part in the following discussion, ROUBAUD and BRUMPT, say, in effect, the author's treatment of the subject is very judicial, very tactful and very well documented. In the end the conclusion come to is that although the prevalence of *Pulex irritans* in Morocco and of *Synosternus pallidus* in Senegal may create special infective conditions, it is the *X. cheopis* of the domestic rat which is the really important plague vector. The work of the Plague Commission of India is upheld and particularly that of BACOT and MARTIN [this *Bulletin*, 1914, v. 3, 201] who demonstrated the importance of blockage of the proventriculus by plague bacilli in *X. cheopis*, a blockage which does not occur with *Pulex irritans*.

Due importance is accorded to facts such as the absence of *Xenopsylla cheopis*, but not of plague, in the equatorial Andes and to the complication of the intrusion into epidemiology of sylvatic plague. Many ectoparasites can be rendered plague-infective and human fleas can become infected from man, but, as it is well put by Roubaud, the intervention of domestic biting insects in plague is possible but is not necessary. Girard renders the student of plague epidemiology a great service by this review and its careful conclusion. His own experience relates to Madagascar and he stresses particularly the importance of the " free " rat flea as a factor in the transmission of plague to man. His conclusion is : " The rational prophylaxis of human plague, its eradication from a country will depend, if not on the total destruction of the rat, which is impossible, at least on its removal from the immediate vicinity of man." *W. F. Harvey.*

BLANC, G. & BALTAZARD, M. Quelques remarques à propos du mémoire de G. GIRARD sur les " ectoparasites humains dans l'epidémiologie de la peste. [**Reply to Remarks of GIRARD on the Rôle of Human Ectoparasites in the Epidemiology of Plague.**] *Bull. Soc. Path. Exot.* 1943, July 7, v. 36, Nos. 7–8, 208–16.

Blanc and Baltazard present a reasoned reply to the criticisms of their views by GIRARD (above). Their position is summed up largely in two main propositions : (*a*) The human flea and louse practically always become infected on man in the agonal period. (*b*) The infected flea and louse can transmit plague. Criticisms of these two statements are dealt with point by point. One of the most interesting arguments turns on the fallacy of translating laboratory animal experiment too literally in its application to man. The conditions of laboratory experimentation, say the authors, were favourable to the rat flea *Xenopsylla cheopis* and unfavourable to the human flea *Pulex irritans* ; *X. cheopis* bites rats and guineapigs with avidity, but *P. irritans* will die rather than nourish itself by ingesting guineapig blood. It is no wonder, then, that *Pulex irritans* is unsatisfactory as a plague vector, and even if it has partaken of the septicaemic blood of a plague guineapig, it is extremely improbable that it will again bite this species of animal to transmit plague. Reverse the position, however, if that were possible. Feed *Pulex irritans* on man in the terminal stage of septicaemic plague and set it to bite man. It will now do so with avidity and, it is presumed reasonably enough, would be an even better vector of human plague than *X. cheopis*. So the argument goes on to lead the authors in conclusion to assert : No one can deny the possibility that human ectoparasites can easily become infected from plague patients and can transmit the infection to man.

In reply (in the discussion of the paper) to this presentation of the position maintained by the authors, GIRARD and ROUBAUD refer to the great interest of the data as applied to Morocco and wish to see the subject pursued further, but both of them are evidently not convinced that transmission of plague from man to man without the intervention of a rat epizootic is at all common, or applies to the territories of their own cognizance. *W. F. Harvey.*

MACKAY-DICK, J. **Report on Reactions to Anti-Plague Serum.** *J. Roy. Army Med. Corps.* 1945, Jan., v. 84, No. 1, 33–4.

A description is given in this note of the disturbing reactions produced by antiplague serum. The dose given was 3 cc. of plague vaccine and 5 cc. of serum. Reactions, which were either immediate or delayed (to the sixth day), were urticaria of trunk and extremities, plus, in the more severe cases, swelling of the face, lips, eyelids and tongue and a hoarse voice. Only one of the British contingent of 11 persons escaped, whereas an Indian contingent did not suffer to any great extent. The author makes out a case for a reaction difference between dark skinned and fair skinned races. *W. F. Harvey.*

GIRARD, G. Réflexions sur la vaccination et la sérothérapie antipesteuse de l'homme devant les données expérimentales. [**Inadequate Immunization of Animals to Plague with Production of Pneumonia and its Applicability to Man.**] *Bull. Soc. Path. Exot.* 1943, July 7, v. 36, Nos. 7–8, 218–22.

Girard asks and answers a question of some importance. BATZAROFF (*Ann. Inst. Pasteur*, 1899, p. 365) separated secondary septicaemic pulmonary plague from primary plague pneumonias. He also showed that the treatment of test guineapigs with vaccine or serum, so as to make them partially but not wholly resistant to plague infection, rendered them especially liable to death from secondary plague pneumonia. His results have been confirmed and generally accepted. In Madagascar large-scale vaccination of the population with a living plague vaccine, and serotherapy, have been practised on millions of individuals. It is conceivable then that the pneumonic plague, which is common in Madagascar, might be referable to inadequate immunization. It is possible, too, that inadequate immunization might result in a restoration of the virulence of the avirulent but living organisms used. The reply to this questioning is in the negative and is summed up in the statement that "pulmonary complications have not been any more frequent in the vaccinated than in the non-vaccinated, nor yet any more frequent in patients treated with serum than in those untreated." Moreover, the pneumonic cases of plague have diminished in parallel with, and in the same proportion as, the total number of plague cases under the influence of vaccination. Thus human beings differ entirely from the small rodents in liability to plague pneumonia after insufficient immunization. *W. F. Harvey.*

CHOLERA.

LINTON, R. W. & JENNINGS, R. K. **The Biochemistry of *Vibrio cholerae*. I. Growth Methods.** *Arch. Biochem.* 1944, Feb., v. 3, No. 3, 419–27.

This series of studies had as its ultimate object the development of a simple medium capable of giving massive growth of cholera which could be used directly as a vaccine or for investigation of chemical, physical and immunogenic properties of the cholera vibrio. It was essential also that the medium could be "eliminated after growth had taken place, leaving behind the bacteria and their soluble products of high molecular weight." Such a medium was found with the composition :—$(NH_4)_2SO_4$ 5 gm. ; K_2HPO_4 0·75 gm. ; $MgSO_4$ 0·10 gm. ; peptone 2 gm. ; glucose 1 gm. ; and distilled water to 1 litre. As this medium did not give a colourless product, the peptone was replaced, with equally good growth results, by 15 cc. of tryptic digest of casein. The seeding medium,

80 cc., had the same tryptic digest composition and this culture was of 18-hour incubation. It was found experimentally that an addition of 3·3 cc. of 25 per cent. NaOH per litre produced the optimum initial *p*H of 8·8 in the medium and this amount of alkali was used as routine without further attempt at adjustment. The final *p*H after growth varied between 5·5 and 6·5. A very important part of the technique to produce massive growth was aeration by CO_2 " followed in the earlier experiments by nitrogen and in the later ones by air," with a special cloth bag device to obtain fine diffuse, instead of coarse bubbles. A maximum growth could be obtained on this medium already in 24 hours. " After removing the organisms the liquid part of the culture was readily freed from the inorganic salts and casein digest, leaving the soluble bacterial products of high molecular weight in pure form." *W. F. Harvey.*

JENNINGS, R. K. & LINTON, R. W. **The Biochemistry of** *Vibrio cholerae.* **II. The Influence of Environmental Factors on Growth.** *Arch. Biochem.* 1944, Feb., v. 3, No. 3, 429–38, 2 figs.

In this continuation of the first article [above] the problems of composition of the medium are presented in more detail: (1) *The Influence of Glucose.* The higher the concentration of glucose the more rapid and more prolonged was the growth. An upper limit of consumption of the sugar was found to be 0·3 per cent. when growth ceased because of the accumulation of acid. Any excess of glucose was not utilized. (2) *The pH Changes during Growth.* Optimum growth occurred between 6·0 and 8·0. Periodic neutralization of the medium with alkali during growth gave no increase of the vibrio crop. Thus the conclusion was reached that " the buffer value of the medium would be all important in determining the final crop." (3) *Ammonium Sulphate as a Buffer.* The ammonium sulphate was originally intended to supply nitrogen for the growth of the vibrios, but its activity was largely that of buffering and it " greatly increased the amount of CO_2 which the medium could neutralize." (4) *The Influence of Aeration.* That this was not due to mechanical action or removal of some objectionable volatile substance was tested by substitution of nitrogen for air. It proved inefficacious. Aeration provides the proper concentration of dissolved gases for optimum growth. " An important factor is the presence of sufficient concentration of CO_2, which should be greater than the normal CO_2 content of air." (5) *Casein Digest as a Nutrient.* This serves as a source of organic nitrogen and as a growth stimulant; it was more acceptable for the subsequent treatment of the culture than the equally effective 0·2 per cent. peptone. *W. F. Harvey.*

JENNINGS, R. K. & LINTON, R. W. **The Biochemistry of** *Vibrio cholerae.* **III. Acid Regulation by means of the Carbon-Dioxide-Bicarbonate Buffering System.** *Arch. Biochem.* 1944, July, v. 4, No. 3, 311–18, 1 fig.

It has been found that growth of *Vibrio cholerae* depends on the glucose present in the medium and it is well known that the vibrio requires maintenance of a high *p*H in its nutrient medium, while acidification, or lowering of *p*H, brings growth to a stop. Unfortunately the utilization of glucose for growth results, by fermentation, in the production of acid. Earlier workers have aimed at keeping down this acidification by having $CaCO_3$ present in the medium. Under the conditions of experiment by the authors, which involved continuous aeration of a very simple medium, this addition " did not result in greater yields of vibrios." The object of the authors was to obtain such a heavy growth in a water-clear medium that it could be used as vaccine, which they call the " Biochemical Research Foundation (B.R.F.) direct vaccine." This medium was prepared as follows: a 3-litre flask, provided with bubbling

and sampling tubes, containing 1 litre of distilled water and 15 cc. of casein digest, and stoppered with cotton, was autoclaved ; when it had cooled, 10 gm. of glucose, dissolved in a minimal amount of water, and 12 gm. of sodium bicarbonate were added and the mixture shaken until the bicarbonate had dissolved. As there was some formation of carbonate, CO_2 was bubbled through for a few minutes before inoculation. Inoculation was effected by adding 100 cc. of a vibrio culture which had grown in the author's salt-C-D [casein digest] medium [see above, I & II]. An efficient buffer system was utilized in the medium to retard acidification. This buffer mechanism was based on the establishment of " a carbon dioxide exchange system similar to that in the lung " and depended on the fact that " a considerable reserve of alkali in the form of sodium carbonate can be maintained at a desired *p*H by proper adjustment of the carbon dioxide content of the atmosphere." Aeration of the medium was effected by a " cloth bubbler " device, and CO_2 from a cylinder was mixed with the entrant compressed air. Titration of the culture for its reaction could be done without interruption of aeration, as also could the estimation of degree of growth. Periodic addition of alkali had been ruled out, because the vibrio is immediately sensitive to even transient exposure to high alkalinity. The cholera vibrio could utilize greatly larger amounts of glucose in this new medium than in the old, but utilization did not altogether mean continuous growth. An optimum concentration of glucose, for growth purposes and complete utilization, was 10 gm. per litre (1 per cent.). If 20 gm. were used, about 7 gm. still remained unused after multiplication ceased. This new method gave a fivefold increased yield of cholera vibrios. The culture was killed by the addition of phenylmercuric acetate, and could be " used directly as a vaccine or as a readily purified source of vibrios for chemical and physical studies."

W. F. Harvey.

Paul, B. M. & Chatterjee, B. C. **Pyrogenic Reactions following Intravenous Saline Infusions.** *Indian Med. Gaz.* 1944, July, v. 79, No. 7, 305-7.

Experiments were made in rabbits and in cases of cholera, in which intravenous injections were given of hypertonic or normal saline, of various *p*H values, and made with either freshly prepared distilled water or tap water. These indicate that febrile reactions are produced by pyrogenic substances which are absent from freshly distilled water but present in tap water, or by solutions of high or low *p*H, but not by those about the neutral point. If the solution is more acid or alkaline than the blood can buffer, pyrexia is produced.

Charles Wilcocks.

BACILLARY DYSENTERY.

Felsen, J. **Bacillary Dysentery, Enteritis and Colitis.** *Clinics.* 1944, Oct., v. 3, No. 3, 535–52, 11 figs. [12 refs.]

World-wide surveys, carried out since 1933 by the Dysentery Registry, reveal conclusively that where infectious diarrhoeas are carefully studied the majority appear to be bacillary dysentery.

In the United States in 1933 the reported incidence of this disease was 625, for unclassified diarrhoeas 17,043, for typhoid and paratyphoid 23,349, and for amoebiasis 1,573. Since then a steady and rapid increase in the bacillary dysentery returns has been accompanied by a striking decline in the unclassified

dysenteries, typhoid and paratyphoid, whilst amoebiasis remains uniformly low. But competent observers believe that the reported incidence is but a fraction of the actual incidence.

The remainder of this paper is devoted to a consideration of the pathogenesis and clinical aspects of bacillary dysentery. In acute bacillary dysentery the toxins produced within the lumen are absorbed through the intestinal wall and distributed throughout the body by the circulating blood, to be eventually excreted in a reverse direction through the intestinal wall into the lumen of the bowel. The intestinal lesions are produced during the process of reverse excretion. The anatomical basis for this mechanism is simple. The intestines contain numerous solitary lymph follicles, located partly in the mucosa and partly in the submucosa. The intramural mesenteric vascular arborizations terminate as delicate filamentous networks, about the size of capillaries, which embrace and penetrate the lymph nodules—an arrangement which assures intimate contact between noxious agents, which pass through the capillary wall, and the lymphoid tissue. A three-stage progression of pathological changes can be observed on the first, second and third days of the disease—punctate follicular hypertrophy and hyperplasia, punctate follicular necrosis, discrete and confluent ulceration, and these changes can readily be seen through the sigmoidoscope.

During the first stage the enlarged lymph follicles, bulging through the mucosa, appear to the naked eye as scattered grains of sand on a hyperaemic mucosa ; in asymptomatic types they may not progress beyond this stage. In the average acute case the necrotic centres of the lymph nodules appear like the mouths of tiny diverticula. Then these areas of necrosis gradually become confluent and present the stereotyped picture of bacillary dysentery. Milder cases are just as infective as those which progress to extensive ulceration ; all contacts, therefore, should be examined by sigmoidoscopy and culture. There are no healthy carriers of bacillary dysentery and a patient who excretes dysentery bacilli will always be found to have intestinal lesions.

Receding signs and symptoms do not necessarily run parallel to the healing of intestinal ulcers and the latter may persist for weeks. Recurrences are due to persisting lesions.

Acute bacillary dysentery is primarily an enterocolitis with predilection for the distal ileum and colon and it is stated that chronic distal ileitis (regional ileitis) is the end result of acute ileal involvement, just as chronic ulcerative colitis is the terminal phase of colonic involvement. *P. Manson-Bahr.*

WARIN, R. P. & ALEXANDER, R. S. **Splenomegaly in Bacillary Dysentery.** [Memoranda] *Brit. Med. J.* 1945, Feb. 10, 187.

Splenic enlargement was present in 50 (5·77 per cent.) of 866 cases of bacillary dysentery admitted to a general hospital in the Middle East between August 1943 and January 1944. There appeared to be no other cause than dysentery for the splenomegaly. Clinically, the dysentery was mild or moderately severe, diarrhoea lasting for 2·88 days on the average, and the temperature returning to normal after 48 hours. Of 31 cases in which a culture was made, the Flexner bacillus was grown in 13 (Flexner I in three cases, Flexner II in six cases, and undetermined type in four cases), and in 18 no pathogens were found. The spleen was palpable on the day of admission in 49 cases ; it was one finger-breadth below the ribs in 37 patients, two fingerbreadths in 10, and three fingerbreadths in three patients. It remained palpable for 2–6 days in 43 patients and in the other seven it remained palpable until their discharge on the 15th to 18th day. The leucocytes of the blood showed no abnormality. The authors do not know the cause of the splenomegaly, but think it was non-specific

as Major R. S. ILLINGWORTH informed them that he had seen it in a similar proportion of cases of diphtheria, tonsillitis, scarlet fever, and measles in the Middle East and could find no cause for it. *J. F. Corson.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

PAYNE, A. M. M. **Amoebic Dysentery in Eastern India.** *Lancet.* 1945, Feb. 17, 206–9.

In two years' experience in Eastern India, both in forward areas and base hospitals, 2,000 cases of dysentery were seen of which 1,000 were amoebic. Except in a few cases of hepatic amoebiasis, the diagnosis of amoebic dysentery was not made unless *Entamoeba histolytica* was demonstrated in the stools or typical ulcers seen in the gut.

Bacillary dysentery was diagnosed on the presence of typical "bacillary exudate." Shortage of equipment precluded the use of cultures for diagnosis on any large scale, so those which showed an indefinite exudate were grouped as "clinical dysentery." Some were doubtless cases of healing bacillary dysentery and others of amoebiasis with very scanty protozoa in the stools. The proportion of types of dysentery are given in a table :—

Source of cases	Diagnostic procedure	No.	Bacillary dysentery	Amoebic dysentery	Clinical dysentery
Consecutive cases passing through	One stool exam. Case evacuated to base hospital	149	27 (18%)	47 (31·5%)	75 (50%)
Base hospital ...	Stool exams. with sigmoidoscopy in few cases	380	136 (36%)	193*(51%)	51 (13%)
Base hospital ...	Sigmoidoscopy and stool exams.	500	163 (33%)	282†(56%)	55 (11%)

*Includes 27 double infections. †Includes 38 double infections.

Amoebiasis was 1½ times as common as bacillary dysentery. The stay in hospital in amoebiasis varied from a minimum of three weeks up to several months, usually 28 days in uncomplicated cases, whereas in bacillary dysentery the stay was 7–14 days, usually 8 days. The time lost from dysentery in one unit over a period of eight months averaged 27 days in cases infected with *E. histolytica* and 2–3 days in those not so infected. The mortality from amoebiasis was 0·8 per cent., whereas no death occurred from bacillary dysentery in nearly 700 cases.

Both conditions appeared to be mainly fly-borne ; for instance, owing to the use of wet fuel and an unsuitable incinerator in one unit, large numbers of flies bred in unburned faecal matter and invaded the cookhouse, 100 yards away, with the result that seven cases of amoebic dysentery occurred among 100 men 4–6 weeks after this disaster.

All grades of severity were seen from the very acute with extensive ulceration, 20–30 daily stools, fever and prostration, to the mildest diarrhoeas. One case

of extensive ulceration without diarrhoea or obvious blood or mucus in the stools was recorded. The patient was also heavily infected with subtertian malaria.

At autopsy general peritonitis with thick fibrinopurulent exudate in the right iliac fossa was found. There was perforation of the greatly thickened caecum. Intrinsic massive confluent amoebic ulceration was seen there, and scattered ulcers in the ascending colon and sigmoid.

Amoebic *typhlitis*, closely mimicking appendicitis, also caused concern. The complaint was pain the the right iliac fossa, either colicky or continuous, often occurring after meals, presumably as a result of the gastrocolic reflex. There was usually diarrhoea with blood and mucus, but the most difficult cases were those in which the stools were formed and without mucus. The temperature might be raised to 99–100°F. Tenderness, guarding, rigidity, greatest over McBurney's point may cause suspicion of appendicitis. A thickened caecum is a valuable sign, and also liver tenderness. Rovsing's sign [pain in the right iliac fossa on pressure in the left], hyperaesthesia, and a reduced or absent abdominal reflex may all be found but are inconstant.

Rectal examination may elicit tenderness on the right side, sometimes there is a " velvety touch " and the mucosa is folded redundantly. There may be blood or mucus on the withdrawn finger. The white cell count shows an increase to 10,000–14,000, but the polymorphs are not increased relatively to other cells. If hepatitis is present the total count may be higher, though it may be normal and the polymorphonuclear leucocytes retain their normal proportions. Sigmoidoscopy showed typical lesions in some 50 per cent.

Two cases of amoebic typhilitis were opened under the impression that they were appendicitis. Plastic peritonitis was seen, but no perforation.

Amoebiasis causing dyspeptic symptoms occurred in chronic cases, with pain in the epigastrum, or right hypochondrium, ½–2 hours after meals. Symptoms due to mild hepatitis or reflex pyloric spasm disappear rapidly under emetine treatment.

Amongst 1,000 cases of amoebiasis the following complications were noted :—

Mild amoebic hepatitis	50 per cent.
Acute amoebic hepatitis	3·9 ,, ,,
Hepatic abscess	2·8 ,, ,,
Haemorrhage (severe)	0·2 ,, ,,
Local peritonitis	1 ,, ,,
Perforation (with general peritonitis) ...	0·6 ,, ,,
,, (with abscess formation) ...	0·2 ,, ,,
Rectal granuloma	0·2 ,, ,,

Hepatitis was so common as to become part of the disease. Usually it was mild and responded immediately to emetine. The more severe forms were rarer and graded imperceptibly to liver abscess. They did not respond so quickly to emetine and tended to recur. Amoebic hepatitis, without diarrhoea and with negative stools, occurred in eight cases.

Of 28 cases of hepatic abscess, 20 were in Indians—an unusually high proportion. Out of 700 British troops with amoebiasis 1·1 per cent. developed liver abscess. Out of 300 Indians the proportion was 6·6 per cent. There was one death in an Indian with an abscess secondarily infected with *Staphylococcus aureus*. Of the remaining 27, three were aspirated and all the remainder made good recoveries on emetine alone. The maximum dosage was grains 60 in 120 days ; the average dose was grains 36 in 108 days. Severe haemorrhage occurred twice, in one case associated with perforation and death. The others recovered with emetine and blood transfusion.

Perforation occurred seven times in the caecum and once in the descending colon. General peritonitis followed in six fatal cases, where the gut was

gangrenous and too friable for effective closure ; two of these perforated during emetine treatment. Two perforations resulted in abscess formation behind the ascending colon. Both had secondary haemorrhage after drainage.

Amoebic granuloma of the rectum was seen twice at sigmoidoscopy with large cauliflower masses resembling carcinoma. They responded to emetine and eusol enemata.

As regards diagnosis, the author maintains that the exudate in amoebic dysentery is not characteristic, as an indefinite picture with necrotic pus cells and degenerated r.b.c. is seen in healing bacillary dysentery. Charcot-Leyden crystals are a guide, but were found in non-specific ulcerative colitis and in carcinoma.

With sigmoidoscopy and microscopy of fresh specimens an immediate diagnosis can be made in 80 per cent. of cases. Proctoscopy, if performed gently, is painless and of more value than is generally recognized, as 50 per cent. show lesions in the rectal ampulla. Premedication before sigmoidoscopy is unnecessary unless the patient is very nervous. The knee-elbow position was used for preference.

Results of 500 *Sigmoidoscopies.*

Type of dysentery	Cases	Positive	Negative
Bacillary	163 (32·6%)	160 (98%)	3
Amoebic dysentery (final diagnosis)	282† (56·4%)	226 (80%)	56‡
(1) Appearance diagnostic ...	—	155 (55%)	—
(2) Appearance not diagnostic; diagnosis by stool exam.	—	71 (25%)	—
Clinical	55 (11%)	—	55
Total ...	500	386 (77·2%)	114

†Includes 38 double infections. ‡Diagnosis by stool examination.

Treatment was very largely dictated by the drugs available. For a *primary* case 10–12 injections of emetine grain i (total given being grain i to 1 stone body weight). The injections were divided into two groups of 6, with three days' rest in between to diminish toxic cumulative effects. Then carbarsone 0·25 gm. b.d. was given by mouth for 10 days.

This achieved clinical cure in 50 per cent. (but the author thinks this may be an overestimate). In 40 per cent. cysts were found within three weeks and though carbarsone appeared to clear most of these, 10 per cent. required further emetine or E.B.I. plus chiniofon enemata. Two per cent. resisted all forms of treatment.

Cysts seldom reappeared in the faeces until 10–20 days after treatment.

It was felt that if three courses had been given a further course would be unlikely to cure, so those patients were sent to special centres for the combined treatment with E.B.I. and chiniofon retention enemata.

Relapses became more frequent and more resistant to treatment the longer the infection had lasted. More thorough treatment of the initial attack including the combined treatment might reduce the number of chronic resistant cases. Sulphapyridine or sulphaguanidine *in four-day courses were of great assistance in allaying symptoms, but did not affect the amoebae.*

Various other drugs—kurchi bismuth iodide, " Enterosol " (4–3 iodoxyquinoline), " Amoebiarsan " (similar to carbarsone), " Stovarsol," retention

enemata of eusol, silver nitrate, and " Argyrol " were of some, but inferior, value. Kurchi was of little value.

Myocardial damage from excessive doses of emetine may be missed, if the pulse is not examined after suitable exercise. Response to the erect position may be dramatic and may be associated with cyanosis, breathlessness and faintness. Personal idiosyncrasy is important and myocardial damage is more common in relapsed cases. A falling pulse-pressure is an early sign. Mild cases clear up in 4–6 weeks. E.B.I. can contribute to cardiac damage, though less liable to do so than emetine.

Diarrhoea in emetine and E.B.I. treatments " is not uncommon and must not be interpreted as a relapse of dysentery." Diet makes little difference to treatment.

Results of treatment could only be estimated, as the majority of cases could not be followed up.

Results.

Clinical cure	33 per cent.
Improved with clinical relapses	33 „ „
Frequent relapses	28·2 „ „
Resistant cases	5 „ „
Death	0·8 „ „

These are very disappointing figures and there is grave need for new and more efficient drugs. *P. Manson-Bahr.*

BOMFORD, R. R. **Chronic Amoebiasis in Soldiers.** *J. Roy. Army Med. Corps.* 1944, Dec., v. 83, No. 6, 279–83.

This paper describes the methods employed in diagnosis and treatment of cases admitted to a Military Centre for Tropical Diseases between November 1942 and January 1944. During this period 112 patients were admitted with provisional diagnoses of dysentery or its effects. Of these, 28 gave a reliable history, but no pathogenic organisms or protozoa were found in the stools ; 51 were found to have bacillary dysentery (including acute Sonne dysentery) by isolation of the organisms ; 33 were considered to be suffering from amoebiasis ; of these 17 were officers and 16 other ranks. One had never been out of the United Kingdom and appeared to have become infected in Northern Ireland. The length of history varied from two months up to ten years. Out of these 33, in seven only was recent diarrhoea the principal symptom ; in a few others it had been occasional, but in 14 it was absent altogether. Four had hepatitis ; two with diarrhoea and two without.

Diagnosis was suggested by history of previous dysentery, previous residence in the tropics and subtropics ; the presence of tenderness over the colon or liver ; the naked-eye appearances of the stools, which were occasionally characteristic with blood, mucus and typical odour, but often watery and unformed.

Diagnosis was confirmed by :—

(1) *Microscopic examination of the stools.*—Vegetative *E. histolytica* were found in six and cysts in 24. In searching for the latter much assistance was obtained from Faust's zinc sulphate concentration method. At least three stools were examined by ordinary, and three by the concentration method.

(2) *Microscopical examination of specimens obtained at sigmoidoscopy.*—Scrapings were taken with a Volkmann's spoon through the sigmoidoscope, mounted in normal saline and examined. For this purpose the instrument should be lubricated with mucilage, as the presence of oil droplets makes the scrapings useless for microscopic examination. No amoebae were ever found in specimens obtained from an unbroken surface, but were demonstrated

in smears of bloody mucus seen coming down the sigmoid when no ulceration was visible. In two cases active amoebae were found in scrapings from ulcerations after repeated examination of stools had failed to demonstrate them or their cysts.

(3) *Sigmoidoscopic appearances.*—One case only was diagnosed on sigmoidoscopic appearances alone. This patient gave a history of previous amoebic dysentery followed by mild diarrhoea and aching abdominal pain. He also had a moderate leucocytosis. With specific treatment the symptoms were relieved and the colon returned to normal.

(4) *Response to empirical therapy.*—With this exception, patients complaining of diarrhoea and colonic symptoms with negative faeces and sigmoidoscopic scrapings were not benefitted by specific antiamoebic treatment.

Of the 30 cases in which treatment was recorded, 20 had been treated previously for amoebiasis and 10 had not. Of these 20, seven had received emetine injections, repeated on several occasions. Only seven had previously received an efficient course of E.B.I. and chiniofon retention enemata. Several more had been treated at various times with emetine, stovarsol and incomplete E.B.I. and chiniofon enemata.

The drugs available are emetine, emetine-bismuth iodide, auremetine [combined emetine and auramine periodides], chiniofon, stovarsol or carbarsone, and it is generally agreed that E.B.I. or auremetine by the mouth are the most effective and that simultaneous E.B.I. or auremetine, with chiniofon enemata probably give the highest proportion of permanent cures. Emetine injections usually abolish symptoms, but effects are rarely permanent.

In treatment of these cases emetine injections were used for two purposes; for the treatment of hepatitis in which 12 daily injections were given intramuscularly, and to control diarrhoea in patients with active dysentery, before other treatment was commenced, for which three or four injections sufficed. All patients were treated with a course of E.B.I. by mouth and chiniofon retention enemata for 12 days, followed by stovarsol for 10 days. The minimum dosage, given to those who had received no previous treatment, was E.B.I. grains 2 nightly with 300 cc. 2½ per cent. chiniofon enemata retained for at least six hours.

The *maximum* dosage, to those in whom this treatment had failed before, was E.B.I. grains 3 nightly and 300 cc. of 5 per cent. chiniofon, but most had six days of the lower dosage followed by six days of the higher. Stovarsol was given in doses of grains 4 twice daily. This treatment was rarely depressing. In a few it failed. In the remainder there was noticeable improvement in colour and general condition with relief of symptoms. One developed a generalized maculo-papular rash whilst taking stovarsol.

The immediate results were, on the whole, satisfactory in the case of officers and unsatisfactory in other ranks. Of 16 other ranks, treatment failed completely in three, cysts were still present and symptoms for all practical purposes unaltered after two complete courses of E.B.I., chiniofon and stovarsol, and in two of them an additional course of auremetine grain i four times daily for 10 days. In three more the stools were cleared of cysts for the time being, but symptoms remained. All were discharged from the Service. The reasons for failure in treatment are not fully understood, but possibilities should be considered:—

(1) *Failure of co-operation on part of the patient.*—Those who had treatment before had lost faith in treatment and only wanted to get out of the Army. They were difficult and disgruntled. It was possible that some of them endeavoured to evade treatment.

(2) *Failure of the coating of E.B.I. capsules to dissolve.*—This is probably greatest in warm climates, and undissolved orange-coloured keratin-coated

capsules have been recovered from the stools of patients in this war. When keratin-coated capsules are used the stools should be strained through muslin, and if they are found, the capsules should be crushed and given in a spoonful of jam. A number of cases have been treated in this manner without producing undue nausea or vomiting. Such insoluble keratin-coated capsules have been used extensively in the Army and it is possible that they have been one of the causes of failures.

(3) *Possible induced emetine-fastness.*—Whereas the immediate results of treatment were highly satisfactory in all cases treated for the first or second time, all patients in whom it was unsuccessful had had repeated unsuccessful previous treatments. Therefore emetine-fastness is possible. It is wise to recommend that emetine injections should be used to tide the patient over for a short period till it is convenient for him to have the full combined treatment. Whenever possible, the effect of such treatment should be checked by further examination of the faeces and by sigmoidoscopy. Thereafter the faeces should be re-examined in 3–6 months' time.

[That most of the points which he has emphasized now for over 20 years have been confirmed is a source of satisfaction to the reviewer. The failure of keratin-coated capsules of E.B.I., for instance, to dissolve in the bowel has been recorded by him as well as by many others, ever since the introduction of this drug as a treatment for chronic amoebiasis. It is satisfactory too to learn that they have, somewhat tardily, been withdrawn from use in the Army, for it is more than probable that many failures in treatment have been attributable to this cause alone. This paper once more confirms the fact that attention to details is essential for the successful treatment of amoebiasis, especially under war conditions.] *P. Manson-Bahr.*

WENRICH, D. H. **Studies on *Dientamoeba fragilis* (Protozoa). IV. Further Observations, with an Outline of Present-Day Knowledge of this Species.** *J. Parasitology.* 1944, Oct., v. 30, No. 5, 322–38, 49 figs. on 2 pls. [44 refs.]

The author, who has studied the peculiar amoeba or aberrant flagellate *Dientamoeba fragilis* for a number of years, now gives a general account of this organism, based chiefly on the study of 100 cases of infection which have been diagnosed in his laboratory. He notes that for its identification, training in recognition is probably of more importance than for any other intestinal protozoon. Stained films are nearly always required. On this account the figures of its incidence in many surveys can hardly be regarded as accurate. The normal features of the amoeba are known, but there are many departures from these. They are carefully described. A feature not hitherto recorded is the occasional formation of a peculiar tube-like extension of cytoplasm from the layer between endo- and ecto-plasm. It passes through the ectoplasm and protrudes from the body surface. Its function is unknown, but it is noteworthy that a similar structure occurs in *Histomonas meleagridis*, to which, as noted by DOBELL [this *Bulletin*, 1941, v. 38, 422], *D. fragilis* shows many resemblances. The author holds that in mitotic division of the nucleus only four chromosomes are formed, whereas Dobell maintains there are six. The author agrees with Dobell that the desmose may persist till cytoplasm division occurs. Another feature of resemblance to *H. meleagridis* is the presence of a deeply staining layer of cytoplasm between the ecto- and endo-plasm.

The paper, which is illustrated with 49 figures depicting the many structural variations described by the author, requires to be studied carefully by specialists who undertake the identification of intestinal protozoa. *C. E. Wenyon.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

BURROUGHS, A. L. & HOLDENRIED, R. **Recovery of Relapsing Fever Spirochaetes from *Ornithodoros turicata* (Duges), 1876, in California.** *J. Bacteriology.* 1944, Nov., v. 48, No. 5, 609.

Relapsing fever has been transmitted to guineapigs by the bite of *Ornithodorus turicata* collected in California. The ticks (175) were collected from the burrows of *Citellus beecheyi*, divided into 11 pools, and fed on guineapigs. This is the first record that this tick has been found to be a vector in California.

Charles Wilcocks.

SCHUHARDT, V. T. & O'BRYAN, B. E. **Relationship of Penicillin Therapy to Brain Involvement in Experimental Relapsing Fever.** *Science.* 1944, Dec. 15, 550–52.

The authors have tested the effect of penicillin on relapsing fever infection in rats using a strain of *Spirochaeta recurrentis* (*novyi*) which had only recently been derived from ticks, *Ornithodorus turicata*. The 45 rats used were injected with small doses, 0·01 cc. of onset blood containing 1 to 5 spirochaetes per 100 dark fields, and were divided into nine groups of five each. Five of these groups were treated with penicillin beginning some days after the blood had become positive ; in three groups treatment was begun on the first day of onset ; and one group was left as a control. The animals were subsequently examined for residual brain infections. The 25 rats in which treatment was begun late, and the controls, all showed residual infections, including 7 out of 10 that had received more than 40,000 units of penicillin per kgm. In the early treatment group, the brains of seven out of eight rats were negative. It would appear, therefore, that adequate dosage of penicillin, about 40,000 units per kgm., given early in the treatment of experimental relapsing fever, will not only cause the disappearance of spirochaetes from the blood stream but will prevent residual brain infection in the great majority of cases. [Previous work (see this *Bulletin*, 1944, v. 41, 942) showed that much higher doses are necessary to cure more intense infections.]

E. Hindle.

YAWS.

HELFET, A. J. **Acute Manifestations of Yaws of Bone and Joint.** *J. Bone & Joint Surgery.* 1944, Oct., v. 26, No. 4, 672–81, 12 figs.

This paper, based on findings in West African cases, mostly soldiers, deals with acute lesions that require urgent treatment.

The onset was more rapid, and more pain was suffered than in syphilitic lesions. Duration of symptoms was rarely longer than a week, by which time marked bony changes might be present, resembling septic lesions. In syphilis symptoms are less marked and less acute.

Onset was often related to trauma and was accompanied by fever, rarely high, and widespread " rheumatic " pains which lasted a few days. Localizing symptoms help in diagnosis.

The tibia, femur, clavicle and humerus were found especially affected, but the skull and lumbar vertebrae were also involved and occasionally the bony lesions were generalized. Plantar and palmar lesions did not co-exist with bone lesions, none of which had ulcerated through the skin. The Wassermann and Kahn reactions were positive in all cases.

X-ray films showed cortical thickening and bony expansion with localized areas of rarefaction or cortical rarefaction and periosteal bony deposits. These deposits might resemble those in osteogenic sarcoma or, in the most acute lesions, the " onion-layering " of a Ewing's tumour. [The illustrations are excellent.]

The histo-pathological appearances resembled those of syphilis in the small round cell and plasma cell infiltration and perivascular cuffing, but there was little or no endarteritis obliterans which is so characteristic of syphilis. Yaws lesions were more vascular than those of syphilis and it was suggested that this may account for their more rapid course.

Ganglia lined with oedematous granulation tissue and hypertrophied villous tags, and chronic synovitis with hypertrophied synovial membranes were seen. [No note is made of the number of lesions observed or studied histopathologically.] Ganglia were excised before arsenical treatment was given as they subsided slowly.

There was dramatic response to treatment by Acetylarsan or Novarsenobillon (N.A.B.), or alternate doses of Bismostab and Sulphostab, the pain disappearing in 1–2 weeks and bony lesions showing some resolution in six weeks. [Dosage not given.]

[The lesions illustrated are almost certainly all those of tertiary yaws but the criteria for differentiating from syphilis are rather weak. The most important diagnostic aids are a history of yaws, scars of secondary skin yaws or, failing these, a rural origin of the patient. Similar lesions are likely to occur in any Colonial Service personnel from yaws areas. Medical Officers in charge of such will find this paper very helpful.] *C. J. Hackett.*

LOFGREN, R. C. **Yaws treated with Penicillin. Report of Case.** *U.S. Nav. Med. Bull.* 1944, Nov., v. 43, No. 5, 1025–30, 2 figs.

A case of yaws in a white man was treated with penicillin with a very successful immediate result.

History.—The patient, aged 20, was a ship's cook in the American Navy. In September 1942 he got gonorrhoea in British Samoa and was treated with sulphathiazole orally and with potassium permanganate irrigations ; he denied having had penile sores then or at any other time, and on entering the Navy in February 1942 his blood gave a negative Kahn reaction. In January 1944, in American Samoa, he burned his right forearm and a small ulcer developed and gradually became larger. At this time he had visited native huts and held naked children in his arms, but he did not remember having seen sores on the children. He arrived back in the United States on March 7th, 1944, and on the voyage his ulcer was treated with ointments but continued to enlarge. On April 4th he noticed a " red pimple " on his cheek which became larger and pustular and covered with a yellow crust ; a week later similar lesions appeared on his face, scalp, arms, hands, chest, back, legs and penis. He had no subjective symptoms.

Condition on examination.—He was seen by the author on April 18th, 1944 ; there was a generalized erythematous, papular and pustular eruption with many of the lesions crusted and scaling, and some were on the palms and soles. Some of the papules were pitted where the crusts had fallen off, and on the right cheek there was a granulomatous nodule covered with a yellowish-brown crust which, when removed, disclosed a raspberry-like base. On the flexor surface of the right forearm there was an ulcer about the size of a half-dollar with a granulomatous base. There were a few erythematous erosions and papules on the penis and prepuce. The posterior cervical, axillary, epitrochlear, inguinal and femoral lymphatic glands were enlarged. Spirochaetes resembling *S. pertenuis* were found by dark-ground illumination in preparations taken

from the forearm ulcer and other lesions. On admission to hospital his blood gave a strongly positive Kahn reaction, the red cells numbered 4,290,000, white cells 4,050, with neutrophiles 54 per cent. and lymphocytes 42 per cent., and haemoglobin was 85 per cent. The cerebrospinal fluid showed no cells, protein 0·032 per cent., Kahn reaction negative, colloidal gold curve normal. The diagnosis was yaws.

Treatment.—On April 22nd he was given 20,000 Oxford units of penicillin intravenously and 15,000 units intramuscularly immediately afterwards; then he received 15,000 units intramuscularly every three hours until a total of 1,500,000 units had been given, during 12 days. Serum from the right cheek lesion was examined by dark ground illumination at 4, 8, 18 and 24 hours after the beginning of treatment; spirochaetes were seen at 4 and 8 hours, not at 18 and 24 hours. Four hours after treatment was begun, all lesions, even those which were apparently drying up, had become more prominent and showed peripheral erythema, evidently due to a local shock reaction, similar to a Herxheimer reaction in syphilis. The patient made no complaint and his temperature was normal. At 8 hours the lesions had become still more pronounced and additional erythematous macules had appeared, especially on the face. At 18 hours this peripheral erythema had gone, many crusts had fallen off, and the lesion on the right cheek was smaller. During the next two days involution of the lesions proceeded rapidly, and by the fifth day the yaw on the cheek and all the smaller lesions had entirely healed, and the forearm ulcer, which had been having saline wet compresses, was dry and almost healed, and local treatment was stopped. By the 12th day all the lesions had healed; his temperature, which had been taken every three hours, had remained normal throughout. The Kahn reaction was four plus on May 22nd, one plus on May 29th and negative on June 6th and 9th.

The author states that a prolonged follow-up will be necessary to judge whether a permanent cure has been obtained. *J. F. Corson.*

LEPROSY.

Juon, M. Les derniers cas de lèpre autochtone en Suisse. [**The Last Indigenous Cases of Leprosy in Switzerland.**] *Schweiz. med. Woch.* 1944, July 22, v. 74, No. 29, 795–800.

This paper is mainly of historical interest. In 1898 Jadassohn discovered a focus of leprosy at Guttet, the last case of which has now disappeared. In the middle ages Switzerland suffered severely from leprosy, records of which still exist, and in 1898 four cases were found in Guttet among persons who had never left their village since their birth, constituting an endemic focus of the disease. Two were lepromatous cases in a brother and sister of 10 and 11 years of age, one was a lepromatous case in a man of 47 and the fourth a mixed case in a youth of 17; all four patients were closely related, as shown by a genealogical table. These cases occurred among a population of 200 people in an isolated area. In the village of Feschel, not far away, two other cases had occurred in one family and here the disease was traced back for one hundred years, with a history of seven cases in four generations, only two of which still survived in 1907, by which time three of the total of six verified cases had ended fatally. In 1921 three remained, but in 1922 two new cases were reported, making a total of five. Four of these are described in detail and illustrated by photographs: two were advanced lepromatous and one a third-stage neural case. All these patients had died by 1927, thus bringing the disease to an end.

The persistence for so long of this focus of infection is attributed to the poverty and backward social and hygienic conditions of the inhabitants of these remote villages. *L. Rogers.*

MUIR, E. **Leprosy in Antigua.** (**2nd Report.**) *Leprosy Review.* 1944, Dec., v. 15, No. 2, 35–40.

At this, Dr. Muir's second visit, in July 1944, he is able to report some progress since his first inspection in January 1942 [see this *Bulletin*, 1943, v. 40, 463]. Changes have been made in the Leper Act and Rules on the lines recommended in the former report, and there has been more following of contacts, leading to earlier segregation of infectious cases. This is shown by an increase in the leper home of L1 and L2 cases from 2 to 13 and of L3 cases from 16 to 19, accompanied by a decrease of active nerve cases from 11 to 8, and an increase of the total cases from 37 to 48. In addition, arrangements have been made to place 27 closed neural cases under treatment outside the home. Another 14 arrested cases are living in their own homes under supervision; the total known cases now number 90. Improvements have also been made in the staff, including the provision of a matron with two years' training at the Trinidad Leper Settlement. The patients have gardens, but their diet is still deficient in vegetables and fruit. The cost of segregation amounts to £52 a head annually, including £24 for food. The control of leprosy by up-to-date methods is thus important from the financial as well as from the public health point of view. The difficulty in supplying a properly qualified staff for combating leprosy in such a small island as Antigua, and most of the West Indian Islands, is pointed out, and although the Trinidad settlement is prepared to take a certain number of cases suitable for treatment, there remains the difficulty in persuading patients from other islands to avail themselves of this offer.

L. Rogers.

MUIR, E. **Leprosy in St. Kitts and Nevis.** (**2nd Report.**) *Leprosy Review.* 1944, Dec., v. 15, No. 2, 40–43.

In July 1944 Dr. E. Muir paid a second visit to these islands to see the results of his report on his first visit in February 1942 [see this *Bulletin*, 1943, v. 40, 463]. A new Master of the Leper Home has been appointed after being trained at the Trinidad Chacachacare Leprosarium with advantage, but little other progress appears to have been made. The total cases in the home have only risen from 46 to 49 by the addition of three neural cases. The active lepromatous cases remain at 27, but the new admissions amount to 13 because 10 patients have died in the interval between the visits. There are, however, about 27 known active cases, including 7 or 8 lepromatous ones, outside the Home, and other cases isolated at home require more supervision. The surgery premises are inadequate, a treatment room with running water being badly needed, and more land is needed for cultivation by the inmates. Several of the nerve leprides might be cleared up by intradermal treatment; this also applies to extramural cases. The fact that some fresh cases were detected during a short visit indicates that there are still active cases at large. No mention is made of the regular examination of contacts, which is essential for detecting new cases in an early stage. *L. Rogers.*

MUIR, E. **Second Report on Leprosy in Jamaica.** *Leprosy Review.* 1944, Dec., v. 15, No. 2, 43–9.

This visit was made in October 1944 to follow up the results of a former one in August 1942 [see this *Bulletin*, 1943, v. 40, 462]. In the interval new wards

had been constructed for male patients, which will relieve the overcrowding when they can be opened. An entertainment hall and new kitchens have also been supplied, so some progress in this direction has been made. Unfortunately, the most important recommendation of the earlier report, namely the revision of the Leper Asylum Law to " circumvent its most harmful clauses " and to allow modern methods of leprosy control by finding and treating early uninfective cases at dispensaries, is still awaiting urgently needed action, after having been recommended at three earlier visits by leprosy experts since 1926. The Medical Attendant has not yet been sent for training in leprosy work. Former recommendations for the supply of surgical instruments, a microscope etc., have not been complied with. In respect to leprosy legislation, Jamaica, the largest and wealthiest of the West Indian islands, is behind other British Colonies in this area, and should frame new laws based on those not long ago adopted by Trinidad. Small rehabilitation grants should be supplied to discharged uninfective neural cases. As an example of the need for the early adoption of modern methods it is mentioned that there are 17 known unsegregated lepromatous cases who are living in contact with 47 children under the age of 15 years ! They should be isolated without further delay. Moreover, there are several patients in the asylum who could be rendered fit for discharge before long by efficient intradermal treatment with hydnocarpus oil. A considerable amount of examination of contacts has been carried out, but for such a large island a whole-time leprosy expert must be supplied if good progress in reducing the disease is to be made. That will prove to be an economy in the long run. *L. Rogers.*

VAN DER SAR, A. Lepra en las Antillas Neerlandesas. [**Leprosy in the Dutch West Indies.**] *Rev. Policlinica Caracas.* 1944, May–June, v. 13, No. 76, 169–85, 4 figs. [26 refs.]

The first authentic records of leprosy in the Windward Islands date from 1764. During the French occupation of St. Martin and St. Eustatius a leprosarium was established under the name " Hen and Chickens " [no reason is given for adopting this name]. When the French left, about 1780, the lepers were transferred to one of the islands near Guadeloupe, probably the Isle des Saints. Later, fishermen going from here spread the infection elsewhere. According to EHLERS, leprosy was present in San Domingo in 1500, probably imported by slaves from Africa, but it must be remembered that sailors, chiefly Spanish and Portuguese, visited the islands and might import infection. The slave trade to St. Eustatius began about 1644 ; it may have been earlier, but there exists a letter of that time asking for 200–300 slaves for that island and St. Croix.

In 1801, during the English occupation, a decree was issued for lepers to keep to their own houses ; in 1803 it was made penal for lepers to appear in the streets. The first case known in Saba was recorded in 1840 as having been imported from St. Kitts.

The number of lepers has always been greater in the Windward than in the Leeward Islands. In 1903 the leprosarium at St. Martin was falling in ruins, so it was closed and the inmates were moved to St. Eustatius. In 1920 this was suppressed and since then all lepers of the Windward and Leeward Islands have been sent to the Zaquito institution in Curaçao. To the Leeward Islands leprosy came first, probably from South America *via* Colombia, with the slaves, or was brought by the Portuguese coming with their slaves from Brazil in 1659.

At the beginning of the nineteenth century lepers in St. Martin were treated with the oil extracted from the seeds of *Jatropha curcas* (the Physic Nut tree) ; it has a purgative action like that of croton oil, but not so drastic. Doubtless a certain number of deaths were attributable to it and, on account of the pain

it produced, it never became very popular. Later, chaulmoogra oil was used, with a diet rich in vitamins and with yeast tablets. Treatment with diphtheria antitoxin and toxoid, on Oberdoerffer's theory, was tried but the results were disappointing. Of 26 whose sera were tested by the Wassermann and Kahn reactions, 11 were positive to both, 10 were negative to the former and 12 to the latter, while five and three respectively were doubtful.

A graph shows the number of cases and the population for the years 1869–1944. The year of greatest number was 1876 when the total was 61, of whom 15 were in Curaçao, 28 in St. Eustatius and 18 in St. Martin. On January 1st, 1944, there were 27 in the leprosarium, 18 males, 9 females. All but five were blacks, four were whites and one a half-caste. Presence of the disease was detected in one under 5 years, in five between 10 and 15, in four between 15 and 20, in three between 20 and 25, in one between 25 and 30, in four between 30 and 35, and in nine above that age. As regards type of case, eight were nodular, four nervous, four were macular, and 11 were of the mixed types.

Discharge from the leprosarium was permitted if bacteriological examination was negative for three consecutive years. *H. Harold Scott.*

MONEY, T. D. F. **Abstract of a Further Report on the Oji River Leprosy Settlement, Nigeria.** *Leprosy Review.* 1944, Dec., v. 15, No. 2, 50–52.

This report on the work of 1938 to 1943 amplifies the information in one that was reviewed in this *Bulletin*, 1944, v. 41, 587. This settlement deals with the Onitsha Province of Nigeria, with a population of over one million in 5,000 square miles. In 1943 the central settlement provided residence for 1,187 patients, all highly infective except for some advanced nerve cases requiring special care. In the surrounding territory a number of out-patient clinics provide regular treatment for from several hundred to one thousand earlier cases at each, with a total yearly attendance of 305,793. The province is estimated to have from 20,000 to 25,000 active cases, of which 3,000 to 5,000 are highly infectious, requiring isolation. Some live in villages in which only infectious patients reside, and many more are isolated in their homes.

The child adoption scheme of B.E.L.R.A. provides for about 100 infected children in a special compound, and others are paid for by their parents. The indications are that few patients with active disease fail to attend the clinics in order to obtain treatment, but full surveys have not yet proved possible. Bacteriological examinations of 372 cases in 1941–43 showed: negative throughout 79·2 per cent.; positive throughout 9·4 per cent.; becoming negative, 9·2 per cent., and becoming positive 2·2 per cent. The work has steadily increased in spite of war-time difficulties. *L. Rogers.*

DENSHAM, W. **The New Luapula Leprosy Settlement, Northern Rhodesia.** [Abstract.] *Leprosy Review.* 1944, Dec., v. 15, No. 2, 53–5.

This is a note on the early stages of the organization of a new leprosy settlement in the densely populated Luapula Valley of Northern Rhodesia, a little south of the Belgian Congo border, by an experienced Toc H worker under the superintendence of the doctor in charge of the neighbouring hospital of the London Missionary Society. Buildings are being erected to accommodate 500 patients, with 5,000 acres of land, together with outlying clinics for early cases. Within eight months, over 113 cases have been examined and 60 are attending for injections, and it is hoped to admit 100 patients to the settlement shortly, to make a start in meeting the needs of a hitherto untouched area.

L. Rogers.

SANTRA, I. **The Problem of Leprosy in the Tehri Garhwal State, U.P.** *Leprosy in India.* 1944, Oct., v. 16, No. 4, 118–22.

Tehri Garhwal is an Indian State (Himalayan) situated at the extreme north-west corner of the United Provinces. Like all the Himalayan area it has a much higher leprosy rate than that of the adjoining plains on account of its more humid climate ; at least 138 cases of leprosy from this State were recently found in leper asylums of British India. In 1916 the State authorities began to control the disease and were helped by an ancient custom of using some kind of segregation of advanced cases on the outskirts of the villages. In 1916 orders were issued to enforce village isolation more rigorously and in case of failure the patients were taken by force to a colony opened at Barahat and were maintained there at the cost of the relatives ; but early in January 1917 only 19 inmates were found there in place of an expected number of 117, owing to the failure of the relatives to pay for their upkeep. In 1919 it was ordered that the relatives of the patients should contribute a fixed amount of food when the harvest was ripe, or pay an equivalent in money, but this plan also appears to have failed as there were no cases at Barahat recently.

In 1943 the State authorities asked for the help of the Indian branch of B.E.L.R.A. and a research worker was sent to make a study and a survey of villages known to be infected, with the result that an incidence of 2·05 per cent. was found among 7,082 people examined. Of 117 cases 45 per cent. were infectious. A colony at Munikirti provides accommodation for 157 cases without treatment. Children up to 14 years formed only 4·2 per cent. of the whole and mild tuberculoid cases 20 per cent. Only 16 patients were found to have been isolated outside villages, 11 of them with uninfective neural lesions. It is advised that only infective cases should be admitted to the Munikirti colony, under the charge of a medical man trained in leprosy work, who could carry out treatment. *L. Rogers.*

SHAMA RAO, A. **Leprosy Surveys in Hyderabad, Deccan.** *Leprosy in India.* 1944, Oct., v. 16, No. 4, 123–7, 1 map.

These surveys were carried out within a radius of five miles around existing leprosy clinics. The incidence in the four districts dealt with varied between 0·24 and 0·36 per cent., it was greatest in the lower castes. Lepromatous cases varied between 23 and 47 per cent. and the proportion of children under 15 years of age was below 10 per cent. in all the districts. The number of cases found was from 6 to 30 times as high as the figures for these districts returned in the 1931 census. The author concludes that leprosy is not a particularly serious problem in the Hyderabad State. *L. Rogers.*

SHAMA RAO, A. **A Simple Method for the Preparation of Iodised Hydnocarpus Oil.** *Leprosy in India.* 1944, Oct., v. 16, No. 4, 116–17.

The author quotes the method of preparation of iodized hydnocarpus oil recently advocated by DHARMENDRA and SANTRA (see this *Bulletin*, 1944, v. 41, 1045) and points out that it is not practicable for an officer travelling with little equipment. He therefore used the following simplified method of preparation with satisfactory results :—40 grains of pure iodine are added to 1 oz. 2 dr. of pure ether in a 2 oz. stoppered bottle and shaken well for about a minute. The iodine dissolves and the iodized ether is added to 1 lb. of sterilized and cooled pure hydnocarpus oil. On shaking, the resulting iodized oil is of a brown colour and can be used immediately for injections. On exposure to air or sunlight, the oil loses its transparency and becomes of a dirty green colour after two weeks, but does not show the presence of any free iodine, and no

precipitate forms. Although the author prefers to use the freshly prepared iodized oil, he found the green samples equally effective in treatment and either may be injected subcutaneously or intradermally twice a week in the usual doses; the freshly prepared iodized oil is easier to inject than the pure oil. He has used this method for four years in a very large number of cases of leprosy; early cases of both types respond favourably. *L. Rogers.*

DEGOTTE, J. Recherches sur l'activité therapeutique de l'huile essentielle de citronnelle dans la lèpre. [**Essential Oil of Citronella in Leprosy.**] *Leprosy Review.* 1944, Dec., v. 15, No. 2, 28–35, 1 fig.

The author, working in the Belgian Congo during the war, was unable to obtain sufficient supplies of chaulmoogra oil, so he sought for a substitute. This he found in an oil of somewhat similar constitution obtained from a common Congo plant belonging to the family Cymbopogon, from the thick leaves of which it is distilled, and it contains 65 per cent. of a mixture of geraniol, citronellol, citral and citronellal. The remainder is mainly terpenes. It is sterilized by heating on a water bath for one hour. To diminish its irritant properties one part is diluted with nine parts of cotton seed oil, when it can be injected either subcutaneously or intramuscularly in doses of 1 cc. in the first week, 2 cc. in the second, and 3 cc. per week in the subsequent ten weeks. After an interval of fifteen days' the course is repeated. In larger doses it may be harmful in lepromatous cases. The following results were obtained from this treatment during 1943 :—

Cases	Symptoms Disappeared	Improved	Stationary	Worse
2,328	114	223	1,763	95

The author does not claim that the treatment is a panacea for leprosy, but he considers that the essence of citronella, in his experience, is comparable in its effects with those produced by chaulmoogra oils. *L. Rogers.*

ISWARIAH, V. **Acute Lepra Reaction in Course of Thyroid Medication for Obesity.** *J. Indian Med. Ass.* 1944, Dec., v. 14, No. 3, 58.

LINHARES, H. Estudo sôbre a célula leprosa do rato. [**Study of the Lepra Cell in the Rat.**] *Mem. Inst. Oswaldo Cruz.* 1944, Apr., v. 40, No. 2, 183–9, [17 refs.]. English summary.

As long ago as 1921 GUJO found that carmine and trypan-blue when injected were taken up by lepra cells. The author has now studied these cells and their staining affinities. He took eleven infected rats and divided them into two lots. Five were injected with lithium carmine freshly prepared, at 2–3-day intervals on four occasions: first, 1 cc. subcutaneously, the next two 0·5 cc. intraperitoneally, and lastly, 0·3 cc. intracardially. The remaining six received injections of 1 per cent. trypan-blue, subcutaneously, intraperitoneally and intracardially. The animals were killed at intervals and sections of the tissues stained. It was observed that the cells containing the bacilli were the ones which took on the stain, that these were reticulo-endothelial cells, histiocytes, and the stages could be seen of these cells becoming transformed into the typical lepra cells. *H. Harold Scott.*

LINHARES, H. Possibilidades de transmissão e vias de inoculação da lepra murina em ratos e outros animais. [**Possible Ways of Transmission of Murine Leprosy in Rats and Other Animals.**] *Mem. Inst. Oswaldo Cruz.* 1943, June, v. 38, No. 3, 321–51. [101 refs.] English summary.

There is little original work recorded in this article. It is a well-documented summary of evidence reported in the literature regarding the various points considered. A study of murine leprosy is important on account of the similarity between the lesions caused by it in animals and those found in human infection by *Myco. leprae.* The author first reviews the evidence for transmission by insects, considering *Lucilia caesar, Calliphora vomitoria, Musca domestica, Haematopinus spinulosa, Caelaps echidninus* and others. Though *Polyplax spinulosa* was found to contain many bacilli after feeding on an infected animal, no growth was obtained when these were planted on Löwenstein's medium. Rats were readily infected by feeding on diseased animals and also by contact, the organisms entering by way of a skin lesion. Congenital transmission is not proven ; the evidence for nasal instillation is conflicting, as is that by intradermal inoculation ; intracardiac inoculation produced cutaneous and glandular lesions and later generalization. The opossum, *Didelphys aurita* was the species used, was found to be susceptible and responded to inoculation by subcutaneous injection in particular, but also by the intraperitoneal, pleural and osseous routes. Chickens and pigeons were also infectible intramuscularly, and the former intraperitoneally and *per os*, the latter intravenously.

H. Harold Scott.

HELMINTHIASIS.

GORSSE, P. & ACCART, R. Essai sur le traitement de la bilharziose vésicale. [**The Treatment of Urinary Schistosomiasis.**] *Bull. Inst. Hyg. Maroc.* 1943, v. 3, 5–57. [48 refs.]

This study of the treatment of urinary schistosomiasis was made on 65 recently infested European patients and 147 Africans, in Morocco ; most, if not all, were soldiers. Owing to the exigencies of the war, a few only of the cases could be followed up. After reviewing briefly the life-history of the parasite and the clinical course of the disease in man, with particular regard to its chronicity and relapses, the authors consider the tests by which the therapeutic effect of treatment with drugs may be judged. These tests are classified in four groups : (1) clinical signs—haematuria, cystitis, spermatocystitis, and fistula ; (2) the presence and appearance of the ova in the urine ; (3) the blood picture—eosinophilia and anaemia, and serological reactions (complement fixation and intradermal tests) ; (4) the results of cystoscopy. They conclude that cystoscopy gives the best test. The cystoscopic picture shows four distinguishable conditions representing stages in the course of the disease, but the authors admit that the bladder may show more than one " stage " at the same time. It is important to allow a sufficient interval between the end of a course of treatment and a cystoscopic examination.

In discussing treatment the authors mention electrocoagulation as a useful measure in certain cases, but it is reserved for the specialist and does not enter into the general treatment of the disease. Certain drugs—neoarsphenamine, bismuth, and emetine—have been proved to be useless, yet they are still included in textbooks. Antimony is the only parasiticide which they have used in this study and they limit their observations to three preparations—tartar emetic,

Fouadin, and anthiomaline. All these produced a good immediate result but as time went on a less favourable impression was produced, particularly in the case of tartar emetic. In 57 cases treated by the authors with at least 1·60 gm. of the drug, in four only was no immediate clinical effect seen, but when cystoscopy was used on 19 patients, after two months, eight were improved, seven were in the " intermediate stage " (eggs present), and four were not improved ; after four months there were four relapses, two unchanged and two improved. No definite cure has been obtained.

Fouadin [sodium antimony pyrocatechin disulphonate], though easy to administer and freer from toxic effects than tartar emetic, was also disappointing ; they obtained no cure in 11 cases treated and abandoned its use.

Anthiomaline, in their opinion, is the best of the three drugs, but it is not a sterilizing drug ; in eight cases which they were able to review later there were four relapses.

The authors state that antimony is not a specific for schistosomiasis ; like mercury in syphilis, it is insufficient by itself, and what is needed is to find a series [*gamme*] of parasiticidal compounds to be given together or in succession.

J. F. Corson.

SANABRIA, A. Sindrome de Stokes-Adams por miocarditis bilharziana. [**The Stokes-Adams Syndrome due to Bilharzial Myocarditis.**] *Rev. Policlinica Caracas.* 1944, July–Aug., v. 13, No. 77, 282–93, 3 figs. [34 refs.]

A free translation of the author's summary reads as follows :—

Two patients were admitted to hospital with the Stokes-Adams syndrome, in whom clinical, radiological, electrocardiographic and laboratory examinations showed the presence of bilharzial myocarditis. In the first patient the electrocardiograph revealed auricular fibrillation, complete A–V block, intraventricular block and ventricular extra-systoles. While the electrocardiogram was being taken the patient fainted, and there was transitory ventricular fibrillation. In the second patient there was bilharzial myocarditis, but the mechanism of the syncopal attacks was not clear.

WITENBERG, G. **What is the Cause of the Parasitic Laryngo-Pharyngitis in the Near East (" Halzoun ") ?** *Acta Med. Orientalia* (*Palestine & Near East Med. J.*) 1944, Nov.–Dec., v. 3, No. 6, 191–2.

The word *Halzoun* means " snail," but it is applied to other bodies with a coiled appearance. In the Near East, in Lebanon and Syria, a leech, *Limnatis nilotica*, and a fluke, *Clinostoma complanatum*, are found in the throat of man. The former occurs in water and is taken in by man when drinking such water ; cattle may harbour as many as 30 at a time, man as a rule one only. The latter, the fluke, is about half an inch in length, is parasitic commonly in fish-eating birds and is acquired by man through his eating insufficiently cooked fish infested with the metacercariae of the fluke. Once before a case of human infestation by *Clinostoma complanatum* has been recorded, namely by J. YAMASHITA in 1938 (*Ann. Zool. Japonenses*, v. 17, 563).

Fasciola hepatica has also been incriminated as a cause of *Halzoun*, but on insufficient grounds.

H. Harold Scott.

GIBSON, T. E. **Tapeworm in Freshwater Fish.** [Correspondence.] *Brit. Med. J.* 1945, Feb. 10, 199–200.

The author reports a very mild outbreak of tapeworm infestation of trout in a reservoir in Northamptonshire which occurred in August and September 1944. Thirty-nine plerocercoids were recovered from the peritoneal cavity of one of the

affected trout and were fed to 1 guineapig and 3 rats ; the guineapig showed no signs of infection but all the rats passed eggs of *Diphyllobothrium* in their faeces and finally recovered spontaneously. At the time when the trout were dying, 50 grebe [aquatic birds] also died, but it is not known whether they were infected with *Diphyllobothrium*. Later, over 100 " smaller fish " were caught in this reservoir and 40 per cent. of them were found infected with plerocercoids " of a smaller type " than those recovered from the trout. Attempts to infect rats with these were not successful. *J. F. Corson.*

UNSWORTH, K. **Observations on the Life-Cycle of a Species of Diphyllobothrium found Parasitizing Trout in Great Britain.** *Ann. Trop. Med. & Parasit.* 1944, Dec. 30, v. 38, Nos. 3 & 4, 213–19.

This is an account of Unsworth's work on the life-history of the Diphyllobothriid tapeworm, the plerocercoids of which were discovered by DUGUID and SHEPPARD [this *Bulletin*, 1944, v. 41, 857] in trout and sticklebacks in a South Wales reservoir. Beginning with an infested rat sent to him by Duguid and Sheppard, Unsworth infested, as Duguid and Sheppard did, the copepods *Diaptomus gracilis* and *Cyclops strenuus*, finding that the latter was the more efficient first intermediate host and easier to maintain in the laboratory. He describes the developmental stages in these crustacea. After 16–20 days' development of the larvae in Cyclops, 34 sticklebacks were fed with the infested Cyclops and 22 of them became infested with plerocercoids situated chiefly on the serous surface of the stomach, under the peritoneum and under the liver capsule. Some infested sticklebacks were fed to a single pike, in which a single plerocercoid developed. Plerocercoids from both the infested sticklebacks and the pike were fed to puppies aged 2–3½ months, and the adult tapeworm developed in the puppies, which passed eggs in their faeces. Coracidia from these eggs infested Cyclops.

Unsworth makes the epidemiologically important suggestion that the trout in the South Wales reservoir became so heavily infested (100 per cent.) in so large an expanse of water because they ate infested sticklebacks. He points out that the commoner fish hosts of plerocercoids of Diphyllobothriid species (*e.g.*, pike, perch, wall-eyed pike, trout, burbot) eat other fish, while the less common fish hosts (*e.g.*, grayling, pollan) eat other fish only at times.

Unsworth also received from HICKEY plerocercoids of the Diphyllobothriid species found by HICKEY and HARRIS [this *Bulletin*, 1944, v. 41, 858] in the Dublin area and found that these also developed to maturity in puppies. Since Hickey and Harris found adult Diphyllobothriid tapeworms in gulls and cormorants, this species can apparently develop in both a bird and a mammal. Unsworth could not identify the South Wales species, because he recovered from the puppies only the scolex and some immature anterior segments, but he concluded that this species was too small to be *D. latum*, which infests man. Unsworth also concluded that the Dublin species was certainly not *D. latum*. There is no proof, he thinks, that the Dublin and the South Wales species are the same.

All these workers have submitted specimens of the adult tapeworms obtained by them to H. A. BAYLIS, of the British Museum and BAYLIS [this *Bulletin*, 1945, v. 42, 302] reports that all the tapeworms obtained from the gulls represent one species and all those obtained from the cormorants another. Comparison of the worms obtained from the experimental mammalian hosts by all the workers led Baylis to conclude that all the workers were dealing experimentally with a single species, which is probably *D. dendriticum* (Nitzsch, 1824), which is normally a parasite of gulls. This decision seems to rule out the possibility, hinted at by *The Lancet* [1944, April 8, 475] that the South Wales

species might be *D. latum*, which might be introduced into Britain by refugees from Norway or Poland, as it has been introduced into North America by immigrants and has become endemic there. [The relationship between *D. latum* and the Diphyllobothriid tapeworms of birds needs further study in this country. The larval stages of both occur in copepods and fish and are morphologically similar. There are other recent records of these larval stages in fish. Thus Duguid and Sheppard (*loc. cit.*) state that Dr. PETERSON of Yell informed them that a species of *Diphyllobothrium* is endemic in trout in some of the Shetland Islands; and GIBSON [above] records infestation of trout in a Northamptonshire reservoir with plerocercoids morphologically similar to those described by Duguid and Sheppard [*cf.* also T. HARE, *Brit. Med. J.*, 1945, Mar. 10, 347].

With regard to the infestation of man with *D. latum* in west Ireland, O'CONNOR [this *Bulletin*, 1945, v. 42, 218], discussing multiple infestation of man with this species, states that the first case of multiple infestation was recorded by O'FARRELL (*Irish J. Med. Sci.*, 1930, vi, 542). ANDREWS and OLGIVIE (*Brit. Med. J.*, 1944, June 3, 772) record a case of multiple infestation with *Taenia saginata*]. *G. Lapage.*

MAZZOTTI, L. Observaciones en 10 individuos parasitados con *Taenia saginata*. Presencia de huevecillos en la región perianal y en otras regiones cutáneas. [**Observations on Ten Individuals infested with** *Taenia saginata*. **Presence of Eggs in the Perianal Region and other Cutaneous Areas.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1944, Sept., v. 5, No. 3, 207–13. English summary (8 lines).

The ten individuals examined came from different classes of society. The methods of examination used were: (1) Examination of the perianal region by Graham's adhesive cellulose tape [see comparison of this method and HALL'S NIH swab for the diagnosis of enterobiasis, MAZZOTTI and OSORIO, this *Bulletin*, 1943, v. 40, 617, and description of the NIH and GRAHAM'S swabs, this *Bulletin*, 1942, v. 39, 780]. The author had previously (*Rev. Inst. Salubr. y Enferm. Trop.*, 1944, v. 5, 153) found eggs in the perianal region of 15 individuals infested with *Taenia saginata* and of one infested with *T. solium*; (2) Faecal examination by direct smear, which by itself would, the author concludes, have given a much lower percentage of positives. When direct smears were negative, faeces were also examined by the TELEMANN RIVAS centrifugation method and, in some instances, by the STOLL method [this *Bulletin*, 1923, v. 20, 950].

The results were: Out of 108 examinations of the perianal region of the ten individuals 92 (85 per cent.) were positive. It should be noted that, while nine of the patients were given only 4–9 daily examinations with varying results one patient (No. 26) was given 41 daily examinations, all of which were positive. The same observation applies also to the 131 examinations of 61 faecal samples from the ten patients, of which 96 (73 per cent.) were positive. Here again patient No. 26 supplied 22 samples, of which 58 examinations were done, 86·2 per cent. of them being positive.

Other regions of the skin of three of the patients were examined by the Graham method, five eggs being found in the lumbar region of one patient, nine in the hypogastric region of another and 161 between the neck and knees of the third. Eggs were also found on the underclothes of some patients.

The author thinks that the presence of the eggs in the perinanal region and on the underclothes helps to explain self-infestation and infestation of others with cysticerci of *T. solium*. He thinks that, while most reports of self-infestation with cysticerci of *T. saginata* are doubtful, some are proven (*e.g.*,

Fontan, *Gaz. de Hôp.*, 1919, v. 92, 183, and de Rivas, D., 1937, cited by Faust, *Human Helminthology*, 2nd Ed., 1939, p. 314) and may be explained in the same way.

Mazzotti found that proglottids of *T. saginata* placed in a Petri dish immediately after they had been passed, expelled from their extreme anterior ends, after a few seconds or minutes, a milky fluid full of eggs. He calculated that each expels an average of 97,080 eggs. In stained and sectioned proglottids he noted that the branches of the uterus do not stop at a certain distance from the anterior border as most textbooks say, but actually reach this border, so that, when the proglottid is detached, these uterine branches actually communicate with the exterior. Through them the eggs are expelled. The posterior uterine branches do not reach the posterior border. The disintegration of the proglottid is therefore not necessary for the expulsion of the eggs. The proglottid is, in fact, an organism which actively expels the eggs by its contractions as it crawls about; the pressure of the anal sphincter, which the author suggested in an earlier paper as one cause of expulsion of eggs in the perianal region, is not necessary.

[Podyapolskaya, V. P. (this *Bulletin*, 1944, v. 41, 301) refers to the wide use in Russia of the method of scraping the perianal folds for the diagnosis of enterobiasis; he also recommends it for the diagnosis of infestations with *T. saginata*. Podyapolskaya quotes the work of Shtrom, S. K., who also noted that proglottids of *T. saginata*, crawling in a Petri dish, extrude eggs by channels opening at the anterior border, and leave behind a milky fluid, full of eggs, extruded as a result of the contractions while crawling. *G. Lapage.*

Barnett, L. **Colossal Hydatids associated with Choleperitoneum.** *Med. J. Australia.* 1944, Nov. 11, v. 2, No. 20, 511–14, 7 figs.

This is "the follow-up story of the case described in this journal on December 24, 1927, at page 878" [this *Bulletin*, 1928, v. 25, 461]. The patient, now aged 55 years, fell forward on to a large stone when he was six years old [in 1895 ?] and must have caused a hydatid cyst of the liver to burst into the peritoneal cavity. After being acutely ill for three weeks, he gradually recovered, but after two or three years, his abdomen was seen to be becoming more prominent and this slow increase in size continued for the next 30 years. It was always diagnosed as ascites, probably tuberculous, and attempts at aspiration failed. An operation was declined because the patient said he felt strong and fit to work. Finally his health deteriorated and he was sent to the author in February 1927; he was then gravely ill and had an enormously distended abdomen, measuring 57 inches in circumference, while his weight was 17 stone. Thinking that he had ascites, possibly purulent, the author inserted a fine trocar without result, then a larger one (1 mm.), still without escape of fluid, and finally a 2mm. trocar produced unmistakable shreds of hydatid cyst which were further identified by microscopical examination. The Casoni and R.C.F. tests were positive but eosinophilia was only 2 per cent.

Operation was performed on February 24th, 1927, and daughter cysts, varying in size from cherries to coconuts, were evacuated, filling bucket after bucket, until 50 litres (11 gallons) at least were removed. The abdominal viscera were all matted and crowded behind a false membrane about 3 mm. thick. The wound healed in 10 weeks and the patient, then weighing 12 stone, was able to resume his work as a shepherd.

After three or four years, two cysts were observed growing in the lower part of the abdomen, but the patient refused operation for 16 years, being then

aged 55. The second operation was performed on September 5th, 1943 ; the two cysts, about the size of foetal heads, were opened and drained, and the patient was discharged well on November 23rd, 1943.

At the second operation the peritoneum was found to have returned to its normal state as regards its structure and relation to the viscera. Another point of interest is that the two cysts had taken 16 years to grow to the size of foetal heads. *J. F. Corson.*

i. Lane, C. **Threadworm Infections, Prevalence, Pathogenicity, Periodicity and Prevention.** *Lancet.* 1944, Oct. 14, 511–13. [32 refs.]

ii. Pakenham-Walsh, R. **Threadworm Infections.** [Correspondence] *Ibid.*, Nov. 4, 612.

i. Clayton Lane has here brought together a large body of information about *Enterobius*, and shows that there is still much that is unknown. For instance, the events in its life-history between entry into the nose or mouth, and arrival in the rectum remain a subject for speculation. Infection is very widespread, as investigations in the United States and Britain have recently shown, but the curious fact that American Negroes show lower infection rates than the white race is somewhat puzzling.

The pathogenicity of this worm is debated, especially in relation to the appendix. The fact that it and its eggs have been found in abscesses about the rectum is explained by Lane as a sign that it will travel to seek conditions suitable for oviposition (usually on the skin outside the anus) and that it will oviposit wherever those conditions are favourable. Lane sees a nightly periodicity in its habit of parturition similar to that of the periodic race of *Wuchereria bancrofti*, and promises further evidence based on examination of the studies of Professor F. W. O'Connor.

Prevention of infection is shown to be difficult, especially in regard to air-borne infection ; it will probably be a matter of treatment on a large scale, but the ideal drug has yet to be found. The infection is usually trivial, and of the two drugs mentioned, gentian violet may cause intestinal irritation, and phenothiazine may be dangerous. " No drug is yet known that is deadly to the worm yet less risky to man than is the infection. It needs finding."

ii. Pakenham-Walsh has used methylene blue (grains 3, t.d.s. for a week) with apparent success in two adults. *Charles Wilcocks.*

Pigoury, L. A propos d'une " épidémie " de trichinose à Beyrouth (Liban). [**Concerning an "Epidemic " of Trichiniasis at Beyrouth, Lebanon.**] *Bull. Soc. Path. Exot.*, 1943, Mar. 10 and Apr. 14, v. 36, Nos. 3–4, 88–94.

The occurrence of human trichiniasis at Beyrouth between December 1939, and March 1940 was reported by B. Saad (*Presse médicale*, 1940, v. 48, p. 556) and by P. Millischer and Y. Dubarry (*Biologie médicale*, 1942, v. 32, 23). Discussing this outbreak, Pigoury recalls that Wortabet (cited by E. Brumpt, *Précis de Parasitology*, 1936, 5th ed., p. 1055 [without reference and mentioned also by Strong, R. P., Stitt's *Tropical Diseases*, 6th ed., 1942, p. 1241]) recorded Trichinella " fifty years ago " [Brumpt in the 5th ed. gives no date] in a boar in Southern Lebanon. This suggests infestation of the wild fauna of this district, especially the rat, which is very abundant there.

In 1940 the Army Veterinary Laboratory found that " a notable proportion " [no figures given] of rats of Beyrouth were infested. It is unlikely that trichiniasis died out after Wortabet's record of it ; it was probably not recorded because rats and pigs were not examined and no human case was suspected. Human infestations may, however, be latent and there may be no symptoms in

the rat or in even well-fattened pigs harbouring a heavy infestation. The most important reason why trichiniasis may not have been recognized in Lebanon is, however, the small consumption of pork there. Before the French occupation practically no pigs were reared and even after it they were reared only for the needs of Europeans and some Lebanese Christian families. For the last ten years only about 2,000 head were consumed annually, which allows hardly six pigs a day for a million people. Pig-rearing is practically confined to the Beyrouth district.

Only a few human cases were recorded in the 1939–1940 outbreak. [No figures are cited.] These cases were not confirmed by biopsy or by skin or serological tests. Rumour magnified the extent of the outbreak and there was a considerable decrease in the demand for pork. The authorities, under the impression that pigs infested themselves by eating faeces of infested animals, ordered the slaughter of pigs wherever *Trichinella* was found, and of all the pigs at one piggery at Beyrouth, which was situated near an abattoir and a refuse depot, the pigs being fed almost entirely on waste from the abattoir and on material from the refuse depot, which contained carcasses of dead rats. This amounted to a " veritable experimental infestation " of these pigs. During the mass slaughter at this piggery between January and March the Army Veterinary Laboratory recorded that 15 per cent. of about a thousand pigs examined were infested. The trichinized meat was destroyed by the authorities, but carcasses not condemned were allowed to go to market at a time when fear of infestation has greatly reduced the demand for pork, so that great waste occurred at a time when wartime feeding of the people was difficult. Later the Army Veterinary Laboratory was required to examine all carcasses, with the following results: May to December 1940, in Beyrouth and district 1,234 pigs were examined and 16 were positive (1·3 per cent.); January to September 1941 (when the French evacuated the Levant States) 1,273 pigs were examined in the same area and seven were positive (0·54 per cent.).

These figures represent, Pigoury thinks, the average infestation better than the 15 per cent. recorded from the Beyrouth piggery mentioned above. The infestation of pigs was thus moderate. The author quotes the following percentage infestation of pigs in other countries : Germany 0·05 to 0·1, Bulgaria 3·2 [*cf.* Brumpt also 5th ed., p. 1,055], Rumania 0·15, America 4, 5 and 8 [Craig and Faust, *Clinical Parasitology*, 3rd ed., 1943, 233, quote Ransom's (1916) estimate that 6 per cent. of American hogs are positive]. In some Lebanese piggeries, 30, 60 and 100 kilometres from Beyrouth, including Damascus and Aleppo, no *Trichinella* were found, but the number of examinations was admitted to be quite insufficient. Thus trichiniasis in Lebanon seems to be confined to the Beyrouth district, to which pig-rearing was, at the time of writing, also confined ; but if pig-rearing spreads elsewhere, trichiniasis will probably spread with it.

Sarcocystis was found in 30–40 per cent. of the pigs examined. [The remarkably good results of the assumption by the Royal Army Veterinary Corps, of responsibility for meat inspection and also for administration of livestock depots and the rearing of animals for the supply of meat to Allied armies throughout the Middle East (see *Vet. Rec.*, 1944, Nov. 18, 447, and *Nature*, 1945, Jan. 13, 60) must have altered the situation considerably since the French evacuation of the Levant.] *G. Lapage.*

Mönnig, H. O. **Trichinosis in South Africa.** *South African Med. J.* 1944, Dec. 23, v. 18, No. 24, 420.

Trichiniasis has never been found in domestic animals in the Union of South Africa ; as, however, the methods of examination were formerly inadequate to

show light infestations, the authors used the digestive method. Pieces of the diaphragm muscle of pigs (about 5 gm. from each pig) were cut up and digested for 24 hours or longer at 37°C. in 300 cc. of normal saline containing 0·15 gm. of papain per 100 gm. of muscle. The liquid was then poured into a funnel provided with a wire gauze diaphragm covered with cheese cloth. After a few hours a few drops from the bottom of the funnel were drawn off and examined.

During four months, 1,352 pigs were examined in this way with negative results. As the pigs came from a large area of the country they were regarded as representative of the greater part of the Union, and it was concluded that trichiniasis must be absent or very rare in the Union. This view is supported by the fact that raw pork is very rarely given to pigs in South Africa.

J. F. Corson.

SPRUE.

FREIS, E. D. & MATER, D. A. **Intrahepatic Obstructive Jaundice following Mapharsen, with Development of a Spruelike Syndrome.** *J. Amer. Med. Ass.* 1944, Dec. 2, v. 126, No. 14, 892–4, 1 fig.

The case recorded in this communication resembles others in a series of cases of postarsphenamine icterus published by HANGER and GUTMAN (*J. Clin. Invest.*, 1939, v. 18, 261; *J. Amer. Med. Ass.*, 1940, v. 115, 263). A negro, aged 27, who was found to have positive Kahn and Wassermann reactions, was treated with Mapharsen and a bismuth compound; after the third injection jaundice developed and gradually became more intense.

As laboratory tests pointed to obstructive jaundice a laparotomy was undertaken 33 days after admission to hospital, but no obstruction was revealed. A biopsy of the liver, taken at this time, showed distension and plugging of the canaliculi, with biliary thrombi. The syndrome of obstructive jaundice was evidenced by a steadily deepening icterus with clay-coloured stools, without enlargement of liver or spleen, with negative urine urobilinogen, immediate direct van den Bergh reaction, elevated serum cholesterol, negative cephalin-cholesterol test, no increase of prothrombin time, adequate excretion of hippuric acid and normal serum protein partition.

But after the laparotomy it became evident that this was an example of intrahepatic post-arsenical obstruction as originally described by Hanger and Gutman. The prolonged clinical course and the onset with erythema and fever following the third injection of an arsenical were identical with the syndrome described. A sprue-like syndrome supervened during the gradual disappearance of the jaundice. Thus the previously normal glucose tolerance curve became flat and this abnormalty could be ascribed to faulty absorption by the intestinal tract.

The probability that such a deficiency existed was emphasized by the appearance of voluminous greasy stools containing large amounts of fat during the time that the bile was reaching the intestine as well as by the low figure of the blood calcium.

The demonstration of trypsin and lipase in the duodenal contents suggests that the steatorrhoea was not due to deficiency of pancreatic enzymes.

It is of interest to note that a similar intrahepatic lesion has been observed in some cases of steatorrhoea in infants. *P. Manson-Bahr.*

HAEMATOLOGY.

SINGH, B. **Nutritional Macrocytic Anaemia amongst Vegetarians in Forward Areas in the Middle East Campaign.** *Indian Med. Gaz.* 1944, Nov., v. 79, No. 11, 531–5.

Five cases of macrocytic anaemia occurring in vegetarian Indian soldiers in the Persia and Irak Force were studied by the author.

The initial red-cell counts ranged from 1·40 to 1·75 millions per c.mm., the colour indices from 1·0 to 1·2 and the mean-cell diameters from 7·6μ to 7·8μ [technique not stated]. Normoblasts were present in all the cases [presumably in the peripheral blood] while megaloblasts were seen in only one case.

In three of the patients the gastric juice was examined and found to contain free hydrochloric acid. Laboratory examinations for malaria and worm infestation were negative throughout. The van den Bergh test was also stated to be "negative." The sternal marrow was apparently not investigated.

The clinical manifestations were those of anaemia in general, no special signs of nutritional deficiency being noted. The ages of the patients are not mentioned, but it is noted that three of them were soldiers of ten years' service.

The response to treatment is difficult to analyse from the data presented, since it is evident that in all five cases admission to hospital was followed by vigorous blood regeneration. No details are given of the diets received by the patients. Two of them were treated with iron supplemented by a single blood transfusion; one of these also received oral liver extract for four days. The other three patients were given oral or parenteral liver extracts over varying periods. Examination of the protocols, however, provides little reason for believing that the liver therapy played an essential part in maintaining the subsequent haematopoiesis.

The author points out that the patients, of whom three were Rajputs and two Jats, came from communities whose staple diets of fresh milk and ghee normally provide important sources of vitamins; whereas on active service this was replaced by dried or evaporated milk, which is likely to result in impaired vitamin intake. He concludes that the cases of anaemia under consideration probably resulted from dietary deficiency, but whether the deficient factors were primarily proteins or vitamins could not be established.

[Such examples of severe anaemia, presumably nutritional in origin, provide enviable opportunities of advancing our understanding of the fundamental causes of defective haematopoiesis. The attainment of this object, however, calls for the application of modern haematological methods in conjunction with planned therapeutic trials.] *L. J. Davis.*

VENOMS AND ANTIVENENES.

POPE, C. H. & PERKINS, R. M. **Differences in the Patterns of Bites of Venomous and of Harmless Snakes.** *Arch. Surgery.* 1944, Nov., v. 49, No. 5, 331–6, 8 figs.

The authors performed experiments with *Crotalus atrox*, *Ancistrodon piscivorus* and *A. mokasen*, making the snakes bite plasticine and plastic cylinders approximately the size of the human wrist, and a gelatin cast of a hand.

They conclude that the reptiles bite and do not stab. Under the conditions of the experiments, the objects bitten were marked by the teeth of both upper and lower jaws. *B. G. Maegraith.*

SERGENT, Et. Action d'un sérum préparé avec du venin de vipéridés du genre *Cerastes* sur l'envenimement dû aux vipéridés du genre *Vipera*. [**The Action of Anti-*Cerastes* Serum in Poisoning by Snakes of the Genus *Vipera*.**] *Arch. Inst. Pasteur d'Algérie.* 1944, Mar., v. 22, No. 1, 16–17.

The Viperidae of Algeria are of the genera *Cerastes* (*C. cornutus* and *C. vipera*) and *Vipera* (*V. lebetina* and *V. ammodytes*).

The antivenene prepared against snakes of the genus *Cerastes* will cure 90 per cent. of animals given a lethal dose of the homologous venoms, but will also cure 65 per cent. of those given a lethal dose of the venom of *V. lebetina*. The practical conclusion is that if the proper antivenene against *Vipera* species is not available for a person bitten by those snakes, the *Cerastes* antivenene may be used with some prospect of success. *Charles Wilcocks.*

WILLIAMS, E. R. & DAVIES, A. B. **A Case of Adder Bite.** [Memoranda.] *Brit. Med. J.* 1945, Feb. 17, 223.

SERGENT, Et. Sérothérapie antiscorpionique (septième note). Observations médicales reçues pendant l'année 1943. [**Anti-Scorpionic Serotherapy. Seventh Note; 1943.**] *Arch. Inst. Pasteur d'Algérie.* 1944, Mar., v. 22, No. 1, 18–39.

The scorpion has been identified during 1943 in only 56 of 380 recorded cases of scorpion sting :—*Prionurus australis* 48, *P. amoureuxi* 1, *P. hoggarensis* 1, *P. liouvillei* 3 and *Buthus occitanus* 3. In that year the condition of 104 of these patients was classified as grave (24 being almost *in extremis*) ; 78·8 per cent. of these were cured by antivenene injection. Since 1936, 83·5 per cent. of 1,428 persons in a grave condition from scorpion sting have recovered after having received antivenene. Of those who succumbed in spite of antivenene, it is known that more than half either received insufficient dose, or were treated too late. *Charles Wilcocks.*

SERGENT, Et. Sérothérapie antiscorpionique de l'emploi du sérum antiscorpionique en injection rectale contre l'envenimement scorpionique. [**Scorpion Antivenene** *per rectum*.] *Arch. Inst. Pasteur d'Algérie.* 1944, Sept., v. 22, No. 3, 177–8.

Scorpion antivenene injected per rectum has no curative action after scorpion sting. Rectal saline injection does not reinforce the action of antivenene.
Charles Wilcocks.

SMITHERS, R. H. N. **Contributions to our Knowledge of the Genus *Latrodectus* (Araneae) in South Africa.** *Ann. S. Afr. Mus.* Cape Town, 1944, v. 36, Pt. 3, 263–313, 1 pl., 2 folding maps & 20 figs. [79 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, Jan., v. 33, Pt. 1, 12].

Most of the cases of illness or death due to the bite of females of *Latrodectus indistinctus*, P. Camb., in South Africa occur during the harvest season in the grain lands of the coastal belt of the Western Province. During this season, when the spiders are particularly numerous, reaping operations destroy or expose their nests, and they build new ones under the sheaves lying on the stubble to dry. The men who stack these collect several under their arms, and so may disturb the spiders and cause them to bite. During the 1936 harvest, a survey of a considerable area showed that one of every six sheaves had a nest on the underside. A detailed account is given of the bionomics of this spider,

including the method of building the nest, mating and depositing the eggs and the development of the young within the egg-sacs and their dispersal, with short notes on *L. geometricus*, Koch, which has only once been recorded as causing illness by its bite and has a much less potent venom than *L. indistinctus*. It is considered likely that both species occur throughout South Africa ; their known distribution there is shown on maps.

The author also describes both sexes of *L. geometricus* and *L. indistinctus*, discusses and figures the abdominal pattern of the immature stages of the latter and distinguishes a new variety, *L. indistinctus* var. *karrooensis*, which appears to occur only in the high parts of the Karroo, on the basis of differences in abdominal pattern and coloration in the adults and differences in the nests and webs. He considers that *L. concinnus*, P. Camb., is a synonym of *L. geometricus*, since examination of the types showed that they agreed in every respect but darkness of colour, and every variation from pale grey to black has been found in the field.

SERGENT, Et. Essais de sérums antivenimeux contre le venin d'abeille. [**Trials of Antivenenes in Bee Stings.**] *Arch. Inst. Pasteur d'Algérie.* 1944, Sept. v. 22, No. 3, 175–6.

Neither scorpion antivenene nor a serum prepared against *Cerastes* is active against bee venom. *Charles Wilcox.*

TROPICAL ULCER.

PROC. ANN. GENERAL MEETING OF ASSAM & NORTHERN BENGAL BRANCH BRIT. MED. ASS., SHILLONG, 4th–7th NOVEMBER, 1943. 42–7. 1944. Calcutta : Indian Tea Association. **Discussion on the Epidemiology and Treatment of Naga Sore.** [LEWIS, J. A. ; LAPPING ; BURKE ; MCCOMBIE ; SHORTT ; JELLISON ; & others].

In this discussion of Naga sore [which is presumably the same as tropical ulcer, see this *Bulletin*, 1944, v. 41, 614] the impression given by several speakers is of the great importance of the infective element in the epidemiology of this disease. Lewis, Lapping, and others give instances of labourers returning, from work in other areas, to tea gardens in which Naga sore was not at the time prevalent, and of the occurrence of other cases in the tea garden population shortly after the introduction of the infection to the community. McCombie refers to hospital transmission, in which a compounder transmitted the infection to a simple cut, and Choudhury mentions multiple sores, in which, presumably, the discharges from one infect the skin elsewhere. The importance of initial trauma is recognized, but Lewis remarks that the contact cases he has seen were in persons of poor physique, and malnourished. Lapping remarks that we know no more at the present time than was apparent 30 years ago. He also thinks that malnutrition, especially of the skin with its terminal blood supply, is a factor, and assumes that the infective agent is the anaerobic fusiform bacillus. *Charles Wilcocks.*

PATTANAYAK, G. C. **Tropical Ulcer in Angul, Orissa.** *Indian Med. Gaz.* 1944, Nov., v. 79, No. 11, 521–6, 1 chart.

Cases of tropical ulcer were rare, if present at all, in Angul until recently when they began to appear in labourers introduced from Assam. Since May

1942, when the author saw his first case, the number rose to a peak in August–September ; then a steady decline set in for the ensuing 7–8 months. Of 90 cases, the subject of this study, all but two were males [but the relative numbers at risk are not stated]. The poorer and lower social groups were mostly attacked ; those higher in the social scale, under very similar conditions, largely escaped. As usually observed, the ulcers were commonest on the legs, in those debilitated from malnutrition, malaria, hookworm, etc., and started in some local trauma which became infected. Organisms found were very varied and numerous : staphylococci, streptococci, Vincent's spirillum *Fusiformis fusiformis*, and diphtheroids (never the true Klebs-Loeffler organism, as in Veldt sore). If left untreated they were very indolent and slow to heal. Various forms of treatment were tried but no specific cure was found. Sulphapyridine applied locally got rid of the organisms, but seemed to retard rather than to hasten healing ; moreover, sulphanilamide, which was cheaper, gave equally good results. NAB [Neoarsphenamine] was not effectual. In the indolent stage copper sulphate proved useful, as did 2 per cent. perchloride of mercury ointment, but not in the final healing stage. In short, sulphonamides in the earlier stages, applied locally (not internally), and copper sulphate later gave the best results. Permanganate of potassium and acriflavine proved useless in any stage. *H. Harold Scott.*

Irvine, C. **Treatment of Ulcers by Plaster Casts.** [Memoranda] *Brit. Med. J.* 1945, Jan. 27, 120.

The author writes from the Meru district of Kenya, where the standard of living is very poor, the people heavily infected with yaws, and the incidence of ulcer high. " Food shortages periodically lead to outbreaks of ulcers, some of which approximate to a nutritional type ; others are simply yaws, and no doubt many are of mixed type." No attempt was made to differentiate these, nor was it necessary, because they were equally intractable to the usual local treatments (eusol, foments, cod liver oil, elastoplast, copper sulphate, carbolic), and reacted equally well to plaster of Paris. All patients received arsphenamine and bismuth injections, a good diet, tonics and treatment for worms (if required).

Local treatment consisted of cleaning or scraping the ulcer, application of powdered sulphanilamide in some cases, covering with lint on which Zipp [this *Bulletin*, 1944, v. 41, 77] has been smeared, and enclosing in plaster. As a rule, in two or three weeks the plaster could be removed, when it was found that the ulcer had become clean, sloughs had separated, and the area was ready for grafting. A very striking change was noticed in the patients within two or three days of the application of plaster : the pain was relieved, the temperature fell and the mental attitude changed from despair to cheerfulness. [Grindlay, this *Bulletin*, 1944, v. 41, 777, also advocates plaster in the treatment of tropical ulcer.] *Charles Wilcocks.*

MISCELLANEOUS DISEASES.

India. Proceedings of the Conference of the Medical Specialists Central Command and North-Western Army and of the Joint Meeting with the Civil Medical Officers Punjab held at Lahore in February, 1944. 150 pp. 1944. Allahabad : Supt., Printing and Stationery, United Provinces.

This is a report of the proceedings of a Conference at which about 75 Army medical specialists were present. It contains more than 150 pages of closely

printed matter, most of which is of great interest and importance. An adequate summary within a reasonable compass is quite out of the question. The conference must have been of immense value to all who were present, and the report deserves the widest circulation among medical officers in India and the Far East.

Anaemia and Malnutrition were dealt with as a single subject, and no less than 17 of the specialists took part in the discussion. It was generally agreed that malnutrition constituted the basic condition, in which malaria, the dysenteries, and hookworm disease readily caused the three main types of anaemia so prevalent among the Indian troops. Deficiency of the Wills factor in the diet caused the macrocytic nutritional anaemia which appeared to be the same as the macrocytic anaemia of pregnancy; deficiency of iron caused microcytic anaemia; and deficiency of both these factors caused the combined or "dimorphic" anaemia. In many cases defective absorption of these factors seemed to play the chief part so that large doses of crude liver extracts of the "campolon" type, or large doses of ferrous sulphate by mouth, or combined treatment by both of these drugs, had to be given. But even with adequate specific treatment of these kinds there were many failures, which were attributed to keeping the patients on "hospital" diets. One speaker had obtained a startling degree of improvement in the results by opening a special kitchen in which voluntary workers, all of them Indian ladies, prepared tasty dishes containing the necessary articles of food, such as eggs, butter, milk, chicken, liver, fish and yeast. Several speakers advocated whole-blood transfusions for severe attacks; unfavourable results were mentioned, but these were attributed to faulty technique. The great prevalence of the anaemias among "Indian Other Ranks" was attributed to the recruitment of many of these men from areas where malnutrition was prevalent, but several speakers were critical of the rations supplied to the Indian troops. It was pointed out that the British soldiers in India suffered little from the anaemias, probably because of the larger meat ration.

Diseases of the Typhus Group were discussed at considerable length, and mention was made of the recent occurrence of a large number of outbreaks, which were rather unhappily described by some speakers as "endemic" types. Most of the outbreaks appear to have been of the mite-borne and tick-borne types, though there was a pronounced degree of reluctance to attribute particular outbreaks to individual vectors, and there was evidence that occasional cases of flea-borne typhus occurred in many parts of India.

Some of the outbreaks were as follows:—

(1) In Ranchi (Bihar), between 27–12–42 and 14–2–43, there were 35 cases among British troops doing field exercises in jungle country. Two of the patients were officers; these reported having been bitten by ticks, none of the other patients admitted having been bitten by any "insects" except mosquitoes. The agglutination reactions were of the "indeterminate" type.

(2) In and near Calcutta 156 cases were seen in 1942 and 1943, including an outbreak with 49 cases in two Indian regiments stationed at a village 80 miles from Calcutta; all these 49 cases were of the *OXK* type, but no eschar was detected on any of the patients. Most of the other cases seen in Calcutta were also of the *OXK* type, but a few were of the indeterminate and *OX19* types, and some were negative to all three *Proteus OX* organisms.

(3) More than 300 cases occurred in the 14th Army on the Assam-Burma border during the last four months of 1943; all were of the *OXK* type, and in 15 per cent. of the "British-Other-Rank" patients there was an eschar with lymphangitis. The case-fatality rate was about 7 per cent. A "*K*" strain of rickettsia was isolated from one patient. In this outbreak 130 cases occurred within a few weeks in two companies of a British battalion operating on the

slopes of a hill on which palm trees were growing. These were the only palm trees " for many miles around."

(4) A small outbreak, in which 11 cases occurred during November and December, 1941, among troops doing jungle training near Bombay, was of an exceptionally mild type. The agglutination response was of the *OX2* type in six cases (maximum titre, 1–1,250). It was negative in the others. The rash appeared at, or soon after, the onset. This outbreak was suspected of belonging to a special type.

(5) An outbreak of 11 cases was mentioned as having occurred at a Prisoner-of-War Camp at Bairagarh (? locality) " with a high mixed *OX2* and *OX19* rise in agglutinins in nine of the cases."

(6) The occurrence of about 400 cases of Q fever at Dehra Dun (United Provinces) in 1941–42, was mentioned by Lt.-Col. PASRICHA. " The diagnosis was clinical, confirmed later by highly suggestive agglutinations done by Burnett in Australia." [No further information is given of this remarkable outbreak.]

(7) In the Maldive Islands 214 cases of the *OXK* type were seen between May and December 1943. An eschar was seen in some of the cases.

(8) It was stated that " quite a number of cases " of tick typhus were seen in Arakan in 1943. There was a varying degree of agglutination of all three *Proteus OX* organisms ; in two cases a " hard tick " was found on the patients.

(9) In 1943 there were 165 cases in the Central and Southern Commands, " of all three endemic types."

(10) The only occurrence of louse-borne typhus recently reported in India was a mild outbreak in Peshawar City among the civilian population, in 1943.

The Dysenteries.—The importance of immediate expert examination of perfectly fresh stools was stressed. Three speakers reported excellent results in bacillary dysentery from the use of sulphapyridine, which was given when sulphaguanidine was not available. There was general agreement on the desirability of giving a generous diet as soon as possible. One speaker referred to " the pernicious use of salts " in treatment.

[This dictum ought not to remain unchallenged. There is a general tendency among the younger physicians to regard the saline treatment as being discredited, and it is high time that carefully-controlled tests should be carried out before this time-honoured treatment is discarded. LEISHMAN and KELSALL have recently convinced themselves that " saline treatment has definite value." (This *Bulletin*, 1944, v. 41, 1063)]. It was stated that Dr. DAS GUPTA, Director of the Calcutta School of Tropical Medicine, had examined the stools of 300 " British Other Ranks " who had lived about one year in India [and who presumably were free from symptoms]. After a single examination the rate of infestation with *Entamoeba histolytica* was found to be 26 per cent. (cysts only, 17 per cent. ; cysts and vegetative forms, 7 per cent. ; vegetative forms, alone, 2 per cent.). This high rate was suspected to be due to contamination of the Calcutta water supply by sewage.

Tropical Eosinophilia.—The association of this condition with asthma was mentioned as existing in a group of 12 cases ; in six of these special enquiries were made regarding the residence of the patients, and it was found that only one had lived near the sea ; the other five had lived near large rivers or canals. It was stated that Dr. BERGER of Bombay, insisted on the need for a course of at least eight injections of " N.A.B. ", if relapses were to be prevented.

Malaria.—Brigadier COVELL contributed a note on treatment. He was opposed to the intramuscular administration of quinine, especially in debilitated and wounded patients. When adequate doses of quinine by mouth failed to act it usually transpired that the drug had not been taken in the doses prescribed. The U.S.A. Army had recently adopted a standard treatment consisting of five

doses of 0·2 gm. of mepacrine on the first day and three doses of 0·1 gm. on each of the following six days. With each of the doses on the first day 10 grains of bicarbonate of soda were given. Suppressive treatment should be started a fortnight before entry into a malarious area ; when this was impossible a dose of 0·2 gm. of mepacrine should be given daily for 4–5 days to begin with. While pamaquin [plasmoquine] greatly reduced the relapse rate in chronic benign tertian, its effect on relapses occurring within the first four months was not so pronounced, so that in certain areas its use was left to the discretion of the medical officers.

Several of the specialists at the meeting expressed concern at the large number of cases of blackwater fever that occurred after the standard courses of pamaquin; all of these cases had been in Indian or Burmese patients, and it was suggested that the doses were too large for light-weight persons. Some speakers referred to the large percentage of relapses that occurred after the standard army treatment, and examples were given of evasion by patients ; in one instance it was found that 50 per cent. of the patients admitted for malaria while they were supposed to be taking suppressive treatment had no mepacrine in their urine ; similar evidence of evasion was found in 20 per cent. of a group of 1,000 men.

It was stated that a study of the case sheets of patients who had died of malaria showed that the diagnosis and treatment were often delayed one or two days longer than was necessary.

The Dengue Group.—An Indian speaker proposed the adoption of the name "dengue group of fevers," and the inclusion of sandfly fever in this group under the name "phlebotomus dengue." His views on the subject of the fevers of the dengue group were strikingly similar to those long held by the reviewer, and apparently they were formed independently.

Kala azar.—One specialist dealt with the diagnosis of the disease in Europeans in India ; he had seen 10 cases in 1943 among British Other Ranks. The aldehyde test was negative in all the cases. The features common to every case were : pyrexia without toxaemia ; enlargement of the spleen ; and progressive leucopenia. Leishman-Donovan bodies were found by sternal puncture in eight of the cases, but in the other two spleen puncture was needed, and even then it was only after prolonged search by an expert that a single parasite was found.

Sprue.—Reference was made to what appears to have been an explosive outbreak in which more than 100 cases were said to have occurred among British soldiers in the Chittagong area during 1943 ; all recovered when placed on a suitable diet. No clinical description is given of these attacks, and it seems doubtful whether they were cases of classical sprue.

Other subjects discussed were: neurology, psychiatry, tuberculosis, the typhoid fevers, radiology, drugs, medical training, and the recently established Review Medical Board.

Lieut.-General Gordon Wilson, Director of Medical Services, in his opening address said that one of the chief objects of the Conference was to promote the drive "to secure better clinical standards in the hospitals." To have done so much within three days to achieve this object is certainly a feat which reflects great credit on him and all concerned in organizing the Conference.

John W. D. Megaw.

Manson-Bahr, P. E. C. & Guyer, O. K. G. **The Diagnosis and Management of Pyrexia in Wartime (with special reference to Africa).** *J. Roy. Army Med. Corps.* 1944, Oct., v. 83, No. 4, 172–6.

Although this paper has been written with special reference to Africa most of its contents apply to fevers of the tropical and subtropical world in general. By judicious selection and economy in words the authors have managed to deal in four pages with a surprising number of problems of diagnosis and treatment.

Malaria is rightly given first place among the diseases that are discussed. A sharp distinction is made between the malaria of life-long residents in areas of high endemicity and the malaria of recent arrivals in infected localities. The disease is seldom a serious problem among those who have become immune by repeated attacks; in them the finding of parasites does not necessarily mean that they are suffering from malaria as their chief disease, and it is only when their resistance has been broken down by some intercurrent illness that the infection is likely to demand urgent measures. In non-immunes malaria is an emergency which calls for immediate diagnosis and prompt treatment; the disease may be of serious importance even in cases in which parasites cannot be found, and the correct procedure is to give quinine at once unless malaria can be excluded. The Tanret test should be carried out to find whether the drug is being absorbed; if quinine is not being excreted by the urine an intramuscular injection is advised. [Many malariologists believed that a negative Tanret test usually means that the drug has not been taken in the prescribed doses.]

Examples are given of the help that can be obtained from repeated counts, total and differential, of the leucocytes.

In connexion with amoebic fever the authors state that " the only practical method of diagnosis is the discovery of *E. histolytica* cysts in the faeces, and added to this may be response to emetine." [Here again it might have been well to point out that the finding of cysts in patients who have lived for a long time in an area where amoebic infection is common is on a par with the finding of malaria parasites in comparable conditions. So large a percentage of the inhabitants harbour cysts that the presence of these loses much of its significance. If, however, the emetine test is carried out, as is suggested by the authors, there will be few failures in the management of this important disease.

The numerous practical hints contained in the paper will be very helpful to medical officers who have limited experience of tropical fevers.]

John W. D. Megaw.

TREU, R. **Pseudo-Tuberculosis of the Lungs with Eosinophilia, or Benign Eosinophil Leukaemia.** *Indian Med. Gaz.* 1944, Nov., v. 79, No. 11, 511–14, 4 figs. on pl. No. 23.

The author has seen and studied several cases of this interesting pulmonary condition associated with high eosinophilia and gives details of some of them in the present paper. With exception of the eosinophilia the symptoms are very variable: there may be no fever or it may be high, to 104°F., especially after injections of the curative arsenic; lung symptoms may be altogether wanting or may be severe without radiological signs; on the contrary, there may be gross radiological changes, even with absence of lung symptoms; the onset may be sudden with symptoms of acute asthmatic attacks, or there may be a history of " bronchitis " for several months.

Details of six cases are given, each illustrating one or more of these points and so stressing the differences between them. All showed a high eosinospilia; in one it was up to 80 per cent. in a total count of 26,000. One, the last to be related, is of special interest because pulmonary tuberculosis was present also.

The author discusses the suggested aetiology, in particular allergy and the existence of lung-mites. He quotes as favouring the allergy theory FRIMODT-MÖLLER and BARTON [see this *Bulletin*, 1941, v. 38, 539] and WEINGARTEN [*ibid.*, 1943, v. 40, 407]. [But the writer of the former article stated: " much in the clinical entity points to allergic origin, chiefly because the eosinophilia dominates the syndrome described. But it is possible that there may not be a single agent which causes such a condition, but several." In the words of

WEINGARTEN : " At first an allergic state was thought the most likely explanation, but as more cases were examined, this interpretation could not be accepted "]. Lung-mites, as found by CARTER, WEDD and D'ABRERA [this *Bulletin*, 1945, v. 42, 73], may account for some cases with respiratory symptoms, but not for such as have no signs, clinically or radiologically.

The author states that it is " obviously an infectious disease accompanied by fever, swelling of the lymph-glands and eosinophilia " [but he brings forward no definite evidence in proof of this, and the statement is purely a *petitio principii*. Lastly, is it wise to use the term " Pseudo-Tuberculosis " for a condition in which there may be no fever at any time, in which lung symptoms may be absent, and when actual tuberculosis of the lung may co-exist ?] *H. Harold Scott.*

VISWANATHAN, R. & NATARAJAN, B. **Cold Agglutination in Tropical Eosinophilia.** *Lancet.* 1945, Feb. 3, 148.

Sixty-six cases of tropical eosinophilia have been observed ; the sera of 61 were tested for their titre of cold agglutinins and five cases of atypical pneumonia and 39 cases of other conditions were also tested. Titres from one in 16 to one in 2,048 were observed in 87 per cent. of the tropical eosinophilia cases, 90 per cent. of the atypical pneumonia cases and 33 per cent. of the cases of other diseases. Strong positive titres (greater than one in 256) were seen in 44 per cent. of the tropical eosinophilia cases and in three of the five atypical pneumonia sera.

[A misprint in the table makes it appear that 77 per cent. of the other diseases had a similarly high cold agglutinin titre. The figure should be 7 per cent.]

Titrations were read with the naked eye. Dilution tubes had been allowed to stand overnight at a temperature of approximately 8°C. *John F. Loutit.*

MILLER, H. **Transitory Lung Infiltrations accompanied by Eosinophilia. Report of a Case.** *New England J. of Med.* 1945, Jan. 4, v. 232, No. 1, 7–10, 3 figs. [23 refs.]

SCHRAMM, M. **A Fever Epidemic with Eosinophilia.** *Acta Med. Orientalis* (*Palestine & Near East Med. J.*). 1944, Sept.–Oct., v. 3, No. 5, 146–8.

The usual history of those attacked in this outbreak of thirty cases [the population is not given] is that after a prodromal period of 12–24 hours the onset is sudden with chill or actual rigor, malaise, a temperature 38·5–40°C. for 3–6 days, with severe general pains, nausea, perhaps vomiting, severe abdominal pain, facial swelling and blotchy rash of limbs and trunk, quickened pulse, enlargement of spleen in some. All showed marked eosinophilia from 18 to 55 per cent., with total leucocyte count up to 12,000. Temperature fell by " pseudo-crisis " [presumably rapid lysis] on the third to sixth day, but the debility might be considerable and convalescence slow ; eosinophilia to 20 or even 25 per cent. persisted for a month or more. Several of a family might be attacked, but not all simultaneously.

The author in discussing the diagnosis considers trichiniasis, dengue, sandfly fever and tropical eosinophilia. Dengue and sandfly fever are excluded because of the leucocytosis and eosinophilia ; tropical eosinophilia by the course of the disease and the absence of lung signs. Infestation by *Trichinella* he rules out because all in a family did not fall ill at the same time and the eating of pork was denied, though all the patients were Christian Arabs who do eat pork. [The disease might be one of the " dengue group " (no mention is made of the existence or prevalence of *Aëdes*) but the history and symptoms point strongly

to trichiniasis. Judging by investigations which the reviewer has made from time to time into food-poisoning outbreaks, we can rely little on the denial of eating pork ; again, in outbreaks of trichiniasis the fact that *all* in a family are not attacked at the same time has no weight ; all parts of the meat might not be equally infested, all might not eat the same amount at the same meal. To refrain from taking specimens for biopsy, as the author did, because all members of a family did not show symptoms simultaneously was to deprive himself of the surest means of diagnosing trichiniasis or of the chance of excluding it.] *H. Harold Scott.*

GENERAL PROTOZOOLOGY AND PROTOZOAL DISEASES.

i. Adler, S. & Pulvertaft, R. J. V. **The Use of Penicillin for obtaining Bacteria-free Cultures of *Trichomonas vaginalis* Donné, 1837.** *Ann. Trop. Med. & Parasit.* 1944, Dec. 30, v. 38, Nos. 3 & 4,188–9.

ii. Mahmoud, A. H. **Isolation of *Trichomonas foetus* (Riedmüller, 1928) in Bacteria-free Culture by the Use of Penicillin.** *Ibid.*, 219–22. [13 refs.]

These two papers deal with methods of obtaining cultures of trichomonas free from bacterial contamination.

i. Bacteria-free cultures of *Trichomonas vaginalis* were first obtained by Trussell and Plass (*Amer. J. Obst. & Gynaecol*, 1940, v. 40, 883) in 1940, but this was entirely accidental and was due to the fact that the bacteria in a mixed culture died out, leaving the trichomonas alone. The reasons for the death of the bacteria were not determined so that it was not possible to repeat the process. It occurred to the authors of the present paper that penicillin might clear a culture of bacteria. The flagellate was inoculated directly into the following medium—Locke's solution 4 cc., inactivated goat serum 0·5 cc., " septamide " (Heyden) [a Mg derivative of chloramine] (17 per cent. solution) 0·1 cc., and rice starch. Growth was profuse and subculture was made on to the same medium to which sufficient penicillin had been added to give a concentration of 90 units per cc. The trichomonas grew well and was freed from bacteria. Subculture was made into medium containing 230 units of penicillin per cc.

ii. In this paper the author reports that penicillin was successfully used to obtain bacteria-free cultures of *Trichomonas foetus*. The medium employed consisted of inspissated horse serum covered with Douglas meat digest broth to which had been added 2½ per cent. glucose, the *p*H being lowered to 6·8. To this medium before inoculation with material containing the trichomonas, penicillin was added to give a strength of 30 units per cc. The medium was covered with liquid paraffin. The trichomonas grew well and were found to be free from bacteria. Subcultures in the same medium without bacteria were carried on successfully. *C. M. Wenyon.*

GENERAL ENTOMOLOGY.

Wanson, M. Élevage du *Taeniorhynchus* (*Coquillectidia*) *metallicus* Theobald. [**Rearing** *T. metallicus*.] *East African Med. J.* 1944, Sept., v. 21, No. 9, 269–72, 1 pl. facing p. 273.

It will be remembered that the larvae and pupae of *Mansonioides* and related genera are attached to roots and stems of water plants beneath the surface :

they possess piercing organs, which penetrate the internal atmosphere in the plant, and the larvae and pupae derive their oxygen from that source. In general these insects are difficult to rear in captivity, for the broken pieces of plant tend to decompose, and the larvae (though they can swim about) cannot for long use atmospheric air at the surface.

The author rears these larvae in a most ingenious way. He uses a particular type of very cellular packing paper full of air spaces, and immerses strips of this in the water. Larvae pierce the paper and make use of its internal atmosphere. By this method several species have been successfully reared from egg to adult, in the neighbourhood of Stanley Pool, Belgian Congo.

The author describes and figures a number of anatomical points. The subgenus *Coquillettidia* is consistently spelt *Coquillectidia*, which appears to be a pure *lapsus calami*. *P. A. Buxton.*

WANAMAKER, J. F. **An Improved Method for Mounting Mosquito Larvae.** *Amer. J. Trop. Med.* 1944, Nov., v. 24, No. 6, 385–6.

FELDMAN-MUHSAM, B. **A Note on the Conditions of Pupation of *Musca domestica vicina* (Diptera) in Palestine, and its Application.** *Proc. Roy. Entom. Soc of London.* Ser. A. Gen. Entom. 1944, Dec. 29, v. 19, Pts. 10–12, 139–40.

The author points out that in Palestine it is not generally true that full-fed larvae of *Musca domestica* emigrate from damp manure to find a dry environment in which to pupate. Either because of climatic conditions or because of biological differences (the prevalent "house fly" is *M. domestica vicina*), fresh manure dries and forms a crust quickly, and both larvae and pupae are found beneath this crust, at about four inches from the surface. [It seems that the author refers here to cow dung rather than horse manure.]

If cow dung is kept in jars and moistened, full-fed larvae emigrate at night and can be collected in a suitable dish or tray. One may collect larvae for poultry food, using a series of large clay pots filled with dung on successive days, and moistening them when the larvae are nearly full grown. Larvae contain 18·6 per cent. protein, 5 per cent. fat and 5 per cent. other solids (on a wet weight basis); they are rich in riboflavin (3 mgm. per 100 gm.), poor in carotins, and without vitamin A.

In field control one may use a trap on the Baber principle, heaping the manure on a platform surrounded by a gutter, but it is essential to moisten it to cause emigration. *P. A. Buxton.*

MACGREGOR, I. M. **A Case of Accidental Intestinal Myiasis.** [Memoranda.] *Brit. Med. J.*, 1945, Jan. 6, 14.

A normal healthy man of 22, having breakfasted heartily at 7 a.m., collapsed one and a half hours later with cold sweat and desire to defaecate, followed by nausea, vomiting and vertigo. At no time was there abdominal pain. Admitted to sick quarters, he was put to bed, kept warm and given only fluids. Retching was controlled by a few drops of tincture of iodine. A stool passed in the afternoon was loose and full of blood and mucus; no pathogens were isolated in the laboratory. An ounce of castor oil was given and no solid food allowed. He had a temperature of 101°F. and severe headache, but the symptoms passed off by next day. He had a strong desire to eat, which is unusual in cases of acute bacillary dysentery. A stool passed that day contained numerous live and active larvae of *Stomoxys calcitrans* which, in the absence of other pathogens, were assumed to be causative. More castor oil was given and the patient recovered completely by the sixth day, when normal diet was restored. No more larvae

were found after the third day. The larvae probably developed from eggs laid on some fruit which had been eaten without washing or examination.

J. R. Busvine.

MARTIN, R. Sur la pathogénie de la paralysie ascendante à tiques. [**The Pathogenesis of Ascending Paralysis caused by Ticks.**] *Arch. Inst. Pasteur d'Algérie.* 1944, June, v. 22, No. 2, 125–30.

The author presents a new theory to account for the erratic appearance of tick paralysis. He suggests that this phenomenon is rare and irregular because it depends on the development of a certain rare syndrome in the man or other mammalian host. It will be recalled that other theories about tick paralysis have sought to explain it in terms of a problematical virus or of some irregular factor causing the ticks themselves to be toxic under unusual conditions.

In reviewing the main facts the author reminds us that paralysis may follow the bite of a large number of species of Ixodid ticks and that it has a wide geographical distribution : it has, moreover, been observed in many sorts of mammals, most commonly when they are young ; it is commoner if the tick is fixed to the head, neck or region of the spine : an important characteristic is the immediate relief of symptoms if the tick is found and removed. He points out that it is very difficult to reconcile these facts with either of the old views of causation. There is indeed no positive evidence to support the idea that there might be a virus or that there might be some quite unexplained change in the nature of the tick or its saliva. The fact that extracts of ticks or of their eggs are poisonous throws no light on tick paralysis, which is so rare and erratic, even in places where ticks are exceedingly common.

The author goes on to state that medical men have recognized a type of paroxysmal crisis which is due to disturbance of the sympathetic nervous system : the commonest symptoms of this are vasomotor disturbances with or without convulsions. He puts forward the view that the ascending paralysis due to Ixodid ticks might be placed in the same category and points out with truth that, in general, convulsions are much commoner in young animals, *e.g.*, children, than in adults, and that they can be brought on by a number of apparently minor causes. He relates this to the fact that tick paralysis is much commoner in children than in grown-up people.

[The suggestion put forward is certainly interesting, and it must be admitted that the phenomenon is, at present, frankly mysterious and quite unexplained.]

P. A. Buxton.

LABORATORY PROCEDURES.

LILLIE, R. D. **Factors influencing the Romanovsky Staining of Blood Films and the Role of Methylene Violet.** *J. Lab. & Clin. Med.* 1944, Nov., v. 29, No. 11, 1181–97, 1 fig. [20 refs.]

An investigation of various brands of Wright's stain has shown that irregularities of staining are due to the methylene violet content which is present in varying amounts. Furthermore, it has been found that stock solutions of eosinates of methylene blue and the azures in methanol, methanol and glycerin, and other solvents undergo progressive alteration to form the lower azures and methylene violet. The quantity of methylene violet compatible with good staining varies as to whether staining is carried out on a slide exposed to air or in a covered vessel. The presence of an amount of over 4 per cent. is tolerated in

the staining of an exposed slide only if the initial methanol content of the final staining mixture, after the addition of distilled water, is over 20 per cent. If the concentration of methanol is 30 or 40 per cent. the presence of 15 to 30 per cent. methylene violet distinctly improves the staining. It comes about, therefore, that for all concentrations of methylene violet which may occur, an initial methanol content of 25 to 33 per cent. is necessary if good results are to be obtained in exposed slide staining. As alkali polychroming methods are difficult to control, acid chromatic polychroming is recommended. For this 200 mgm. $K_2Cr_2O_7$ (or its Na equivalent) are used with one gramme of 86 per cent. medicinal methylene blue (or 160 mgm. $K_2Cr_2O_7$ if the zinc salt of methylene blue is used). This yields chiefly azure B. Its eosinate is relatively more stable in methanol than eosinates containing higher proportions of azure A such as result from the alkali method. A one per cent. glycerol-methanol solution forms a stable stock solution for dilution as required with plain methanol to 150 or 200 mgm. per 100 cc. for the usual Wright staining technique. The paper is a highly technical one which must be consulted in full by those interested in the chemistry of Romanovsky stains. *C. M. Wenyon.*

HELANDER, S. **Detection of Chemotherapeutics in Thin Sections of Tissue by the Aid of Fluorescence Microscopy.** [Correspondence.] *Nature.* 1945, Jan. 27, 109.

Fluorescence microscopy has not been much used for the demonstration of the presence and distribution of drugs in tissues because the tissues themselves are fluorescent, and the method of preparing the sections might produce changes in the distribution and concentration of the drug. The author froze the tissue in liquid air, dried it over phosphorus pentoxide *in vacuo* at —40°C., then embedded it in paraffin, cut sections and mounted them on slides ready for microscopical examination.

Drugs whose fluorescence is not blue can be shown directly in the section, *e.g.*, Prontosil rubrum and Prontosil soluble have a strong red fluorescence which is visible even in a concentration of 1×10^{-10} gamma per cubic micron. Drugs with a blue fluorescence change colour, in many cases, after heating in an oven, *e.g.*, sulphathiazole turns yellow at 170°C. for 5 minutes, the tissue remaining blue. Other drugs which can be shown by heating are sulphanilamide, sulphapyridine, papaverine, insulin and penicillin. Sodium salicylate, on the other hand, retains its colour after exposure to 200°C. for five minutes, while the tissue turns yellow. No special staining is necessary for the identification of the tissues. *J. F. Corson.*

YOUNG, E. G. & RICE, F. A. H. **Leucocytosis as an Index of Pyrogenicity in Fluids for Intravenous Use.** *J. Lab. & Clin. Med.* 1944, July, v. 29, No. 7, 735–41, 1 fig. [14 refs.]

A simple test for the presence of pyrogenic substances in fluids used for intravenous medication is very desirable, and the authors, having taken note of the fact that the alleged leucocytic response to allantoin in man was proved to be due to pyrogen, have devised a means by which the content of pyrogen in a fluid can be estimated by noting the symptoms, temperature and white cell counts of dogs after injection. The stock pyrogenic solution, used as a standard, was made from a filtered suspension of *Pseudomonas aeruginosa*, which contained 5·6 mgm. of nitrogen per 100 cc. The fluids to be tested were compared with dilutions of this in their effects upon dogs ; 1–20 cc. were injected intravenously.

Leucocytosis was found to be the most sensitive index, but the authors point out that the leucocyte count of dogs varies very greatly ; it is necessary,

therefore, to make counts before and after injection. The level of the leucocytosis produced is approximately proportional to the amount of pyrogen in the more dilute preparations. The lymphocytes do not show a response comparable with that of the neutrophiles. Leucocytosis appears to have been maximal 3–12 hours after injection.

By this means " it is possible to detect the presence of pyrogenic substances at or below the level of concentration which will produce symptoms in man." An increase of 50 per cent. above the original leucocyte count is significant at 6 hours after injection. *Charles Wilcocks.*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

HOODLESS, D. W. **The Central Medical School, Suva (Annual Report for 1943).** *Fiji, Legislative Council. Council Paper No. 17.* 1944, 10–13.

During 1943 there were 48 students in residence, and also six post-graduate students ; of the former 18 were in their first year, 16 in their third, and 14 in their fourth year. There were no second year students because, as a result of the change (in 1931) from a 3-year to a 4-year course, no students were admitted in 1934, 1938 and 1942. Ten administrations, from Fiji to Samoa, are now sending students. The teaching staff comprises one full-time officer and 12–15 honorary teachers.

The Central Medical School has now completed its first 15 years of service, during which it has trained 130 native Medical Practitioners, but 125 others had previously been trained by its predecessor, the Fiji Medical School, in the period 1888 to 1928. *Charles Wilcocks.*

DUGARD, J. H. **Health Education in the Rural Native School.** *South African Med. J.* 1944, Dec. 23, v. 18, No. 24, 417–18.

This article, by a specialist in education, discusses certain defects in health education which, while familiar to all, are too often disregarded. They are : the presentation of health teaching in the form of uninteresting rules ; the failure of the teacher to impart a knowledge of health in place of the usual mechanical recitation of unapplied facts ; the inability of many teachers to realize that " in health education the learner provides in his own person the subject matter." A common failing in many schools is the division into water-tight compartments of subjects all having a direct bearing on health, both individual and communal, such as physical training, domestic science and biology as well as physiology and hygiene.

In the rural Native school the key to the situation is the Native teacher ; all students-teachers take, at least, a two years' course in hygiene. Teacher-training centres are established at missionary institutions, nearly all of which are in Native Reserves. The health and sanitary facilities vary from centre to centre. After training, the teacher is then expected to perform miracles in his school under the depressing conditions only too well known to health officers abroad. By co-operation between the various authorities some progress has been made.

Despite the strong recommendation of the Interdepartmental Committee on Native Education (1935) that Medical Inspectors and trained nurses be appointed for pupils in Native schools, nothing has been done to implement it. On the question of school feeding, a pertinent point is raised concerning the " 2d. per meal per child " as to what should be recommended as the ideal

meal, one which is to protect as well as to fill. Sex education, including instruction about the venereal diseases, is lacking. The article concludes by advocating sound practical steps for co-operation and co-ordinating committees.

E. Cochrane.

McGregor, M. **Health Education for Rural Bantu Children.** *South African Med. J.* 1944, Dec. 23, v. 18, No. 24, 418–19.

The major problems in the schools are poor nutrition and dirt. Amongst school children the author's findings were that, in every age group, the average height and weight records were distinctly less than the accepted average for Europeans. The view that this is due to an admixture with Bushmen and Hottentots is no longer held. It is evident that nutrition plays a part and an experiment has been planned to supplement the diet of rural school children with fats and fat-soluble vitamins.

A point concerning School Feeding Schemes, often overlooked by the non-medical administrator, is particularly well brought out. It is that those who plan school meals in Native schools will miss a great opportunity if they fail to impress upon the children the facts concerning nutrition in such a way that the latter will apply them to home feeding. Correct teaching now will ensure better nutrition of the next generation. The scheme of feeding should be planned to develop in the child a taste for protective foods that will last for life.

The contrast between the standard of cleanliness in school and the actual conditions prevailing in the home make it imperative to train the children to acquire an active dislike of dirt ; this is no easy task since water-supplies are inadequate. There is no relationship between the theoretical teaching concerning bowel diseases and helminthic infestations and its practical application, for few schools possess even the simplest latrine. It is the usual disheartening story of financial and administrative difficulties. The major consideration, the author states, is the provision of health facilities at schools or children's clinics.

E. Cochrane.

Mackie, Janet W. **Adaptation of Public Health Practice to Foreign Cultures.** *Amer. J. Trop. Med.* 1944, Nov., v. 24, No. 6, 331–9.

The author writes from the Medical Section, Health and Sanitation Division, of the Office of the Co-ordinator of Inter-American Affairs, Washington, and very evidently calls upon a good deal of first-hand knowledge in her discussion of a problem which, though largely relating to the South American countries, has the same importance for most backward places. She shows that it is not enough merely to know the medical problems of a country, but that unless the sociological background and the cultural state of the people are taken into account there can be little hope of rapid improvement in the general health. In backward countries the important diseases are profoundly affected by the customs and thoughts of the people, and between backward peoples and the nations which have full educational systems there are differences in the interpretation and evaluation of life which are so fundamental as to create barriers to mutual understanding great enough to interfere seriously with public health and other projects. In these communities, moreover, there is a lack of trained persons who can supervise whatever health measures are proposed, and who can explain and demonstrate them successfully.

The medical problems of South and Central America [and, *mutatis mutandis*, of most tropical countries] are tuberculosis, high infant mortality, typhus, malaria, pneumonia, smallpox, venereal disease, malnutrition and hookworm

infestation ; to deal with such a wide variety of conditions a balanced organization, of which the local full-time Health Officer is the mainstay, is essential. But the Health Officer must have his subordinate staff, and since the members of this staff are those who will come into the closest contact with the community, it is essential that they should be fully aware of the habits of thought of the people. They should, of course, be recruited from the people among whom they will work, but should be so persuaded and trained in the logic of modern medicine that they can gradually break down the beliefs and fetishes which so often obstruct progress. The author makes the very valid point that provision of curative services should be ample, so that the confidence of the people may be obtained and opportunity taken to give elementary health instruction.

The epidemiology of a disease may be modified by the sociological pattern of a community. For instance, in one place in Bolivia, men and boys spend the nights guarding their crops from theft, and sleep, therefore, near streams ; the women and girls remain in the hills. The incidence of malaria in men and boys is markedly higher than in women and girls.' Empirical knowledge of illiterate people concerning the epidemiology of one disease may determine the incidence of another :—anophelines in a certain valley could be controlled, but because the people know the far greater danger (from Oroya fever) they would run if they lived and slept higher up the valley, anopheline infiltration from the uncontrolled higher parts is continuous. Knowledge of facts of this kind is essential to health control.

The author takes note of the fact that native medical art makes a strong appeal to the emotions, and that the detached attitude which serves very well in educated communities may repel the backward peoples. Yet she very rightly insists that it is through logic that modern health information should be introduced. Unexplained rules and regulations are seldom effective, but advice based on explanation accompanied by ample demonstration has a great future. An elementary appreciation of the bacterial origin of disease can be achieved if the people are shown living creatures, in series of diminishing size, by means of lens and microscope [beginning, the reviewer suggests, with such well-known parasites as the intestinal worms]. Simple cultures of bacteria can be made and demonstrated. The people must be taught to protect themselves, but they cannot adequately assimilate their lessons if they are given merely theoretical lectures ; instruction should begin in the schools, for it is the young who can most easily grasp the subjects.

The solution of the problem of approach " lies in a change of emphasis in public health education at professional and postgraduate levels." Curricula must provide instruction for members of the health staffs of all grades, and the author is quite definitely in favour of a plan whereby, although curative services of the highest quality are maintained at key centres, special emphasis is placed on the deliberate training of large numbers of health workers destined to serve the rural areas. (The other programme, suggested by some authorities, that high professional standards, cultivated in urban areas, will gradually diffuse into the rural areas, will not, she thinks, give such good results.) The rural workers so trained for the villages would carry out such duties as vaccination, registration of births and deaths, and certain sanitary duties ; they would give simple treatments and would be trained to instruct the villagers, by demonstrations, in the rationale of disease prevention.

[Many of the duties to which the author refers are carried out, at all levels, in the British Colonies, where in the medical services the local inhabitants are trained to all grades from fully qualified medical men to dispensers, tribal dressers and sanitary inspectors. She is undoubtedly right in emphasizing the need for a logical basis of instruction to the general public. It is probably a mistake to imagine that the sense of logic possessed, for instance, by the

Africans, is necessarily lower than our own. Native races argue well from their premises ; it is these, and not the logical processes, which are at fault. A comprehension of elementary bacteriology is probably not beyond a properly taught child. The author might, perhaps, have added a note on the good effect that may follow the creation of good taste in such matters as cleanliness, housekeeping, and personal habits. Illiterate races are great imitators, and readily follow examples set by others, a fact which may be turned to good advantage, just as it may produce ill effects if the examples offered are poor.]

Charles Wilcocks.

FLOOD, C. A. & SHERMAN, W. **Medical Care in the Belgian Congo.** *Amer. J. Trop. Med.* 1944, July, v. 24, No. 4, 267–71.

This is a brief description of medical organization in the Belgian Congo where great advances have been made in the last 50 years to improve the health of the 10 million inhabitants. More emphasis has been placed upon preventive medicine than on the care of the sick person, and in 1940 there were 188 public health officers [" gardes sanitaires," working under the physicians] in addition to 201 physicians. Most of the large industrial companies employ medical men (there were 81 such in 1940) and there are many medical missionaries. Medical education of the natives comprises a three-year course, followed by two years of hospital work and then by an examination, for the medical assistants ; courses for nurses are held.

The author gives an outline of the position with regard to the main diseases—malaria, yellow fever, trypanosomiasis [largely dealt with by the Foreami organization], yaws, venereal diseases, leprosy [68,000 cases under treatment in 1940], tuberculosis and smallpox. The steps taken to control these do not differ greatly from those adopted elsewhere.

The impression conveyed by the author is of an efficient, progressive organization coping with an enormous problem. *Charles Wilcocks.*

BAER, L. S. & ALLEN, R. R. **Health Status of the Marshallese. A Preliminary Report.** *Amer. J. Trop. Med.* 1944, Nov., v. 24, No. 6, 345–7.

The authors have examined one-fourth of the total population, 1,100 out of 4,500, of the islands and atolls visited. To obtain an accurate idea of the prevalence of disease more will have to be done, but the figures given are suggestive.

Approximately 15 per cent. of children are stillborn, and 25 per cent. of those born alive die before reaching the age of two years. Maternal mortality is high, 10 per cent. The first and last of these are due largely to the fact that there is no prenatal care and mothers are attended by any woman who happens to be near when parturition begins. " On only one island did the native medica practitioner take any interest in obstetrics."

As regards general sanitation (so-called) : Water-supply is rain in cisterns or from brackish ground-wells ; food is scattered on the ground and flies are everywhere ; faeces are deposited ubiquitously. The commonest diseases are : *Yaws.*—75 per cent. of the children under 10 years present active yaws, and juxta-articular nodules and gangosa are seen. *Gonorrhoea* is very prevalent and is commonly called " siplis " which has given rise to the idea that syphilis is prevalent, which is far from being the case. The authors saw no syphilitic chancres, no neuro-syphilis, and the gummatous skin lesions were more probably the result of yaws than of syphilis. They saw two cases of *lymphogranuloma inguinale* with the ano-rectal syndrome. A Frei antigen survey is planned for the near future. *Tuberculosis* is not common ; they found one case of tuberculous

peritonitis and one of laryngitis, but saw only one with signs among 120 adults subjected to fluoroscopy. *Dengue* is frequent; *dysentery*, both amoebic and bacillary, common, and the latter is one of the most frequent causes of death among children. *Leprosy* occurs, but the authors saw only five cases. *Helminthiasis* is not common [no figures are given], flea-borne *typhus* is endemic; tsutsugamushi disease was not seen, nor any *Trombicula*; malaria was not seen, nor any Anophelines. A few cases of neuritis, probably *beriberi*, were met with and one case of cheilitis; many of the natives have spongy, hyperplastic gums which bleed readily. *Scabies* and *fungous infections* of the skin are rife and are ascribed to the use of unsuitable clothing urged on them by the missionaries and now, owing to the war, reduced to the merest rags and very dirty, and there is practically no soap available. *H. Harold Scott.*

WINBLAD, F. A. S. **Dental Survey in the Marshall Islands.** *U.S. Nav. Med. Bull* 1944, Dec., v. 43, No. 6, 1141–4.

GAUD, Jean, SALM, G. & FASSI, F. Parasitisme intestinal chez les écoliers de Fès. [**Intestinal Parasitism among Schoolchildren in Fez.**] *Bull. Inst. Hyg. Maroc.* 1943, v. 3, 87–113. [Bibliography.]

The authors examined the faeces of 518 persons in Fez, Morocco, for evidence of intestinal parasites; 398 were school children of Mohammedan schools in Fez and this study is concerned mainly with them; altogether about 90 per cent. of the children had some species of intestinal parasite.

Helminths.—Of the nine genera which have been recorded in Morocco the authors found only five—*Ascaris*, *Enterobius*, *Trichuris*, *Taenia*, and *Hymenolepis*; those not found were *Ancylostoma duodenale*, *Strongyloides stercoralis*, *Fasciola hepatica* and *Schistosoma haematobium*. *Ascaris lumbricoides* was found in 60–75 per cent., *Trichuris trichiura* in 40–50 per cent., *Enterobius vermicularis* in 5 per cent., *Taenia saginata* in 1 per cent. and *Hymenolepis nana* in 2 per cent.

Amoebae.—The following were found: *E. coli*, 36 per cent.; *E. histolytica*, 14 per cent.; *E. hartmanni*, in two subjects, *Pseudolimax* (*Iodamoeba*) *butschlii*, or *Endolimax nana* [diagnosis doubtful] fairly frequently.

Flagellates.—*Giardia intestinalis*, 8–10 per cent., *Trichomonas intestinalis*, 13 per cent., *Chilomastix mesnili*, about 5 per cent., *Enteromonas hominis*, about 10 per cent. and *Embadomonas intestinalis* in one person. They found also: *Spirochaeta euygyrata* in subjects and *Balantidium coli* in two.

As a rule, intestinal parasites were most frequent in children under 10 years of age, and were more frequent in children than in adults. The association of two or more species of parasite in one person was not, according to the authors' mathematical calculations, simply a matter of chance; some associations were more frequent, others less frequent, than would be expected from calculation. More parasites were found in people who showed no symptoms attributable to them, than in those with symptoms, and the authors give a warning that the finding of parasites is not necessarily a diagnosis in a case of illness.

J. F. Corson.

KEAN, B. H. **The Blood Pressure of the Cuna Indians.** *Amer. J. Trop. Med.* 1944, Nov., v. 24, No. 6, 341–3, 1 fig.

A most interesting study [though unfortunately of a limited number] of the blood-pressure of members of a healthy native race. The Cuna Indians are Panamanians who used to live on the coast of the South American mainland, but more than a century ago, because of a high death-rate, they moved to islands

of the San Blas Archipelago along the Atlantic coast. They live largely on vegetables and fruits (plantains, bananas, yams, mangoes, oranges, pineapples), and sugar cane, supplemented by fowl, deer and peccary [*Dicotyles* (*Tayassu*), of the Family Suidae (*Tayassuidae*)].

The author reports on the systolic and diastolic blood-pressures of 407 Indians, 263 males and 144 females, out of a total population of some 15,000. In the males the average systolic pressure ranged between 109·7 mm. among the 16–25 years age-group and 103·3 mm. at 36–45 years, 108·1 at 66 years and over. Only 10 of those examined were of this age ; in the 56–65 age-group the average was 105·5 mm. [It will be observed with interest that the author confirms what others have found, that the systolic pressure among natives tends rather to fall than to rise with advancing age]. The average for all the males at all ages was 105·4 mm.

Among the females the average was 105·0 mm., and among all those up to the age of 65 years it remained between 104·3 and 105·6 mm. A higher figure (113·7) is given for those over 66 years of age, but this is of no true significance as only three of that age or over were examined. The average diastolic pressure was the same, 69·3 mm., in both sexes. *H. Harold Scott.*

BOOK REVIEWS.

STRONG, Richard P. [M.D., Sc.D., D.S.M., C.B., Professor of Tropical Medicine, Emeritus, Harvard University, etc.]. **Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases.** Seventh Edition in Two Volumes. Vol. I. pp. xvii + 1–871. Vol. II. pp. vii + 872–1747 + xl. With 398 figs. & 3 pls. (2 coloured). 1944. Philadelphia : The Blakiston Company. [$21.00.] London : H. K. Lewis & Co., Ltd. [£5 5s.]

This 7th edition of a famous textbook is dated October 1944. It is largely a reprint of the 6th edition [see this *Bulletin*, 1943, v. 40, 953], with which the pagination corresponds, except that new material has been inserted, sometimes by change to smaller type, sometimes by insertion of paragraphs, and sometimes by insertion of pages numbered (for instance) 904a, b, c and d. The work is therefore slightly bigger than its predecessor, and maintains the same layout and material, with additions which, indeed, are comprehensive and up to date. There has not been much actual rewriting, and by the method of inserting whole pages of new material the flow of the narrative has been made somewhat disjointed—the new material is not always in just the right place. But the matter is there, and no doubt the demand for this work has been great enough to call for reprinting, and the editor is surely right in adding the latest information in whatever manner is most quickly achieved. It remains one of the best books in the world on tropical diseases.

Some idea of the extent of new information now included may be gained from the mention of the diamidines in treatment of trypanosomiasis and kala azar, penicillin in experimental relapsing fever, DDT as a louse insecticide [but the statement that it is effective against louse ova (p. 950a) is incorrect], a description of Bullis fever and an account of recent transmission experiments in kala azar.

There are, however, certain points which may be criticized. On p. 38, *Anopheles darlingi* is noted as an Old World species, and although a short list of Old World species important in malaria is given, such vigorous transmitters as *A. minimus*, *A. punctulatus*, *A. superpictus* and *A. culicifacies* are not included, though they appear in a general table on p. 43. [In this table, incidentally, there are six mistakes of spelling.]

The chapter on leprosy needs additions on the subject of tuberculoid leprosy and on lepromin, but the long addendum on yellow fever brings that subject well up to date. The classification of the rickettsial diseases is not satisfactory; trench fever might well have been placed next to louse typhus, and Bullis fever along with the tick-borne group, rather than with tsutsugamushi, with which it has little affinity. In the account of tropical ulcer more emphasis should, perhaps, have been laid on the underlying element of malnutrition. In the discussion of tsetse in relation to African trypanosomiasis the importance of the different habitats of the different flies is not sufficiently stressed.

But these criticisms are of relatively minor points and should not be regarded as seriously affecting the high standard of this admirable work. The writing is clear and the accounts of disease are such that they present the subjects as they are and as they appear to the practitioner in the field, complex and not yet clearly understood. The mistake of over-simplification has been avoided, and the medical man who buys these two volumes will be able to find much help in the numerous accounts of the findings of other workers. The bibliographies appended to the various sections will help him to study further the subjects which take his interest. The illustrations are excellent.

For those who have not seen the table of contents it is enough to say that all the usual tropical diseases are dealt with and that there are appendices on clinical diagnosis, laboratory procedures, effects of hot climates, personal hygiene, and disinfectants. *Charles Wilcocks.*

Kubes, Vladimir [D.M.V., Director del Instituto de Investigaciones Veterinarias, Caracas]. El *Trypanosoma vivax* Americano, agente de la Tripanosomiasis Bovina en Venezuela, su Comparacion con el del Africa. [**American** *T. vivax*, **the Causative Agent of Bovine Trypanosomiasis in Venezuela; Comparison with that in Africa.**] *3a Conferencia Interamericana de Agricultura, Caracas, No. 1.* Caracas: 1944. pp. xi+124, 20 figs., 10 tables & charts. [85 refs.] [In Spanish; English Summary: pp. 111–117].

Trypanosoma vivax, the cause of Souma in hoofed animals, represents a remarkable instance of a tsetse-borne African trypanosome spreading widely beyond the area of distribution of its natural vector to remote countries. Having been introduced with cattle imported from Africa it has established itself in bovines in Mauritius, the West Indies (Guadeloupe and Martinique), Central America (Panama) and South America (Dutch and French Guianas, Venezuela and Colombia). The only other known example of tsetse-borne trypanosomiasis outside Continental Africa is the occurrence of *T. congolense* in Zanzibar.

The present work is the first monograph dealing exclusively with trypanosomiasis due to *T. vivax*. It represents the results of observations and experimental investigations which the author, who is Director of the Institute for Veterinary Research, has carried out in the course of ten years in Venezuela, where *T. vivax* affects bovines, causing in them a disease known as *Secadera*, *Huequera* or *Cacho Hueco*. From the introduction and the section on geographical distribution it is evident that this disease is more common in Venezuela than is realized outside that country, and it is of considerable economic importance, causing outbreaks, with a high mortality (30 per cent.) among local cattle. The succeeding sections of this book deal with the different aspects of *vivax* trypanosomiasis in Venezuela, where the disease presents certain peculiarities distinguishing it from the African Souma. On account of this and because the monograph contains a number of important new data, it is proposed to deal with some of these points more fully than is usual in a review.

From the account of the aetiology of the disease it is seen that morphologically the South American strain of *T. vivax* (sometimes described as *T. viennei*) is identical with the African ones. Attempts to cultivate this trypanosome proved unsuccessful. There have been no special investigations on the transmission of *T. vivax* in Venezuela but it would seem that various blood-sucking Diptera are capable of acting as mechanical vectors. The author describes numerous attempts to infect mammals with local strains. In addition to bovines which are the only animals harbouring this trypanosome under natural conditions, it is experimentally infective to goats and sheep ; and to a lesser degree to equines, whereas other animals (including rodents) are refractory. In the section devoted to the clinical course it is stated that the disease may occur in acute form, when it gives rise to epizootics with a high mortality, or the infection may be chronic, or even symptomless. The course of the disease depends primarily on the state of nutrition of the herd, being severe in undernourished animals, and mild in those that are well fed. This variation was also confirmed by experimental infections, in which the course of the disease could be favourably modified by improving the diet of the affected bovines. The chief diagnostic methods in *vivax* trypanosomiasis are based on the finding of the parasites by blood examination, lymph-gland puncture, and inoculation of susceptible ruminants. The section on therapy is of especial interest. After reviewing in detail the methods of treatment of *vivax* trypanosomiasis employed in Africa, the author describes his own results in the treatment of the Venezuelan disease with arsenicals and antimonials. While the former were without any effect, the latter proved to be fairly effective, if applied repeatedly in the early phases of the infection. However, the author made the important discovery that " Bayer 7602 " [see this *Bulletin*, 1942, v. 39, 820 ; *ibid.*, 1943, v. 40, 22], which is now employed for the treatment of Chagas's disease, has a highly specific effect on *T. vivax* infections : a single intravenous injection of from 2·5 to 10 cc. of the drug into bovines weighing 100 kgm. results in a complete cure, while a dose of 1 cc. protects from infection.

Some interesting original observations are recorded in the section dealing with immunity. While in African strains of *T. vivax* immunity is of the type known as premunition, in Venezuela it develops in two phases : during the first six months the host becomes premunized but some months later it acquires full immunity, being protected against reinfection for at least two years. Among the methods of immunization tried, the author favours artificial infection of the bovines followed by incomplete treatment with trypanocidal drugs, whereas Schilling's method was found to be of no practical value since the course of the disease in young animals proved to be similar to that in adults. For prophylactic purposes the author recommends the institution of sanitary cordons as well as the treatment of infected cattle with " Bayer 7602." The book is well illustrated by figures, photographs, numerous tables and charts, and there is an adequate list of references.

This monograph is an important contribution to our knowledge of trypanosomiasis in livestock and should be of especial value to veterinary practitioners in the New World. *C. A. Hoare.*

Weinman, David. **Infectious Anemias due to Bartonella and related Red Cell Parasites.** *Trans. Amer. Philosophical Society.* Philadelphia. 1944, Apr., New Ser., Vol. 33, Pt. 3, 243–350, 1 map & 6 figs. on 1 pl. Philadelphia : The American Philosophical Society, 104 South Fifth Street.

This admirable work will probably remain the standard for reference for all interested in *Bartonella* and its congeners for a long time, certainly until further discoveries are made to clear up the few outstanding difficulties, such as the

questions whether the Oroya Fever type and the eruptive phases depend on degrees of host immunity ; what is the nature of development of the parasite in *Phlebotomus* ; the significance of asymptomatic human cases ; to what class does the *Bartonella* group belong ?

Dr. Weinman undertook to gather together all that is at present known of the organisms and the diseases they produce and to put forward the information in a summarized form and he has successfully accomplished his self-imposed task to the lasting benefit of the parasitologist, the bacteriologist, the protozoologist and the clinician.

Human bartonellosis and its animal analogues are important on several counts, among them the fact that the human disease is acquiring a more extensive field of action than has been supposed, that many animals are infected without presenting symptoms, that a combined study of the human and animal form may throw much light on the aetiology, pathogenesis and treatment of blood diseases, while the fact that many animal infections are latent until splenectomy is performed has an important bearing on the immunological function of that viscus.

This monograph serves the two-fold purpose of putting before us in a connected story all that is at present known and pointing out what needs further investigation and thus stimulating research.

The whole work consists of two main parts, in four chapters. The first and last chapters are concerned with human bartonellosis and its public health aspects ; the second with animal bartonellosis, and the third with the closely allied *Eperythrozoon*. One very important factor contributing to the value and success of an up-to-date summary of any condition is a full list of references, with accurate details. This is not infrequently omitted from epitomes in other respects excellent, but is a special feature of the work under review. The documentation is most detailed, the name and year being given in the running text and the full references in a very complete bibliography. To the first chapter, on human bartonellosis, there are over 300 references. The reviewer has not verified them all, but a large number of them are papers which have been abstracted in the *Tropical Diseases Bulletin* and these he has been able to verify and has not found any mistake in them.

The chapter on Human Bartonellosis deals with every aspect of the question : its history, geographical distribution, clinical types, pathology and experimental production, " asymptomatic disease," epidemiology and transmission, latent infection and immunology, and treatment. The chief points in connexion with these are within the knowledge of readers of this *Bulletin* or can easily be looked up, but to have them all brought together in a single work, such as this, is a great boon.

As stated above, control and the public health aspects of human bartonellosis are discussed in the final chapter. The disease is existent not merely in a few endemic foci in South America but may assume epidemicity, as in Peru in 1870 when 7,000 deaths are estimated to have occurred from it, and in the Colombian outbreak, where in a single department 4,000 are said to have died of it out of a population of 100,000. There is no reason to think that infection may not spread far wider and thus become a menace and a public health question of the highest importance. Since an insect vector (*Phlebotomus*) is responsible for practically all infections, and since no effective therapy is known as yet for eradication of human infection, the only available measures of control must consist of those aiming at reducing the numbers of *Phlebotomus* and those directed to avoiding contact between patients and uninfected insects on the one hand, and infected insect and uninfected man on the other. Observation of the habits of *Phlebotomus* has shown that, in certain districts at least, it bites only at night, so workmen (for example, those engaged in building the Puente Carrión over the Rimac

River) are taken out of the district before nightfall, or are transported to the higher levels, for the Peruvian species of *Phlebotomus* are not found where the night temperature is below 55°F., *i.e.* at 8,000 feet or more. Where this is not feasible—and mass emigration would come within this category—*Phlebotomus*-proof buildings should be erected, windows and doors screened, and walls, roof and floors be smooth and solid to prevent breeding and access of the flies ; outside, the filling in of crevices in rocks or masonry. DDT should find a place.

It is to be noted that none of the three species of sandfly present in Peru, *P. noguchii*, *P. peruensis* and *P. verrucarum*, was caught in Columbia collections ; hence, in the latter State either the species involved was different or some other vector than *Phlebotomus* was concerned. Care must be exercised also to guard against the introduction of an infective person into a *Phlebotomus*-infected zone, and of non-immunes into endemic areas.

In Chapter II the Animal Bartonelloses are described and their significance and characters discussed. The position of Haemobartonellae in the Natural Order is not yet determined. They would seem to be most closely related to Bacteria, but, if so, they are of an atypical and distinct group. They differ from *Bartonella*—the cause of human disease—in that they have not been shown to develop outside the blood and do not produce cutaneous eruptions ; moreover, unless resistance or immunity is lowered by removal of the spleen, they do not cause disease ; they are of much wider, perhaps world-wide, distribution, are transmissible by direct blood-inoculation and are readily affected by arsenotherapy. The author deals in turn with *H. muris* (found all over Europe, in North and South America, in the Near and Far East, and in India) which is often present as a latent infection of white rats and may infect mice, rabbits and other rodents and, if splenectomy is performed, sets up a definite macrocytic type of anaemia. The account of the anaemia, its characters and course, the pathogeny and pathology of the disease produced, the morphology, cultivation and results of experimental inoculation of blood and liver suspension or of laked blood into rats, white mice, guineapigs, rabbits, hamsters, monkeys and pigeons, splenectomized and non-splenectomized, are related ; the transmission by the agency of lice, *Polyplax* (*Haematopinus*) *spinulosus*, and the existence of natural immunity or production of acquired immunity are discussed. Instances of natural immunity, that is, immunity in rats in spite of splenectomy, have been shown to be due, in many, if not in most cases [perhaps in all], to the existence of supplementary spleens in these animals.

Haemobartonella canis of the dog is described and considered on the same lines as *H. muris*. It has been seen in Europe, India, Africa, and North and South America. Also *H. bovis* of oxen, *H. microti* of the vole, *H. sturmani* of the buffalo, *H. tyzzeri* of the guineapig, and a few others of undetermined rank are dealt with more briefly. Twenty-one species are named as having been encountered in the literature.

In Chapter III the question of *Eperythrozoon* is debated—its place in the Natural Order and its affiliations. Descriptions of seven named species, their appearances in the blood after splenectomy, the results of experimental inoculation of blood of white mice containing the parasites, *E. coccoides*, into laboratory animals, natural transmission by the louse, *Polyplax serrata*, are all considered at length, and similarly as regards *E. ovis*. Others are treated more briefly, but adequately regarding what is known of them. Animal haemobartonelloses and eperythrozoönoses have a bibliography of nearly 400 references. A well-reproduced plate shows four figures of human bartonellosis, two of the blood, one of an Oroya Fever lymph-node, and one of a section of a verruga ; in these the different types of parasite are seen, the rods, small chains,

dots and rings, and in the Oroya lymph-node, rounded clumps of these within the endothelial cells of a vein. Another figure shows the rods, coccoid and minute ring forms in a blood film of a splenectomized mouse infected with *Haemobartonella microti*, and, lastly, one of *Eperythrozoon coccoides* from a white mouse.

In conclusion, the whole work has been well carried out and, as already stated, until more discoveries have been made it could not, in the opinion of the reviewer, be bettered. *H. Harold Scott.*

GUASCH, Jorge. Paludismo, Kala-Azar, Fiebre Recurrente. [**Malaria, Kala Azar and Relapsing Fever.**] 475 pp., 24 figs. & 10 pls. (6 coloured). Monografías "Miguel Servet." 1943. Madrid-Barcelona: Editorial "Miguel Servet." [27*s.* 6*d.*]

The work here reviewed deals in much, but not too much, detail with malaria, leishmaniasis and relapsing fever as affecting Spain. The first has so many features in common in whatever part of the world it prevails that this monograph will be found to be almost generally applicable. It occupies the first 300 pages, while to kala azar are given 102 and to relapsing fever 55 pages. As this work purports to treat of these diseases as they affect Spain only, remarks on other countries are but occasional or incidental. Nevertheless, as regards Spain at least, this book brings our knowledge very much up to date (1943) and is a most valuable guide.

To pass on to more detail: Malaria is dealt with under the usual headings of geographical distribution in the world (shown in a Table giving the relative percentages of the different infecting plasmodia) and in Spain in particular (a map with varied shading shows the intensity of prevalence), the plasmodia and their life-histories, transmission, clinical pictures, prognosis, diagnosis, treatment (with remarks on the different drugs used), prevention by treatment of patients and of carriers, by antilarval and antimosquito measures and the organization of an antimalaria service (only a couple of pages are given up to this). Some interesting figures are given regarding the effects of malaria in interrupting pregnancy or in killing the foetus. It causes abortion in 8–16·5 per cent. of pregnant women with untreated malaria, in 19–47 per cent. it causes premature birth, and in as many as 32–65 per cent. results in a dead-born foetus. The chief danger is from subtertian malaria.

Among the usual antilarval prophylactic measures, petroleum, Paris green, *Gambusia*, general sanitation, planting of trees, bonification, etc., two others for local application, not widely known, are mentioned, namely cactus paste and Stoxal. Both are French preparations. The former is used in Northern Africa; cactus leaves are sliced, then macerated in water till a mass is formed which decomposes; it is then spread over collections of water where it forms a coating which impedes the respiration of the larvae; it is said to be effective for weeks, even months. The latter, *Stoxal*, is solid triformol which is mixed with dust or fine ash in a proportion of 2–5 per cent. and spread like Paris green. It has the advantage of being harmless to vegetation, to fish and cattle, and is cheaper than Paris green.

A number of remedies for the treatment of blackwater fever are mentioned, including snake antivenene [see also SINGH & SINGH, this *Bulletin*, 1944, v. 41, 927]. None of this is of much use as nothing is said as to details of administration and the doses even are omitted for many of them. The pathological anatomy of malaria is described in half-a-dozen pages.

Kala azar, as it affects Spain, is equally clearly presented; the pros and cons of the identity of human and canine leishmaniasis are put very fairly, but this part contains nothing new or which is not mentioned in Wenyon's classical work. The clinical picture of the disease as it affects children and adults is

given separately and the diagnosis and treatment are adequately described; remarks are made on diseases complicating leishmaniasis, especially tuberculosis (the existence of which, states the author, is common but does not affect the prognosis), diphtheria (which is usually fatal) and whooping cough, measles and scarlet fever which seem to bring about a rapid regression of the kala azar. [Have other writers found this ?] The pathological anatomy is given briefly in three pages.

Lastly, *relapsing fever* not infrequently occurs together with malaria and the former may develop even while full treatment is being given for the latter. García de Cosa has reported several cases of this association, some with *P. vivax*, others with *P. falciparum*. A map shows the distribution of cases in the Lerida outbreak of 1938–39. A useful short table gives the chief distinguishing features of the Spanish tick-borne and the ordinary louse-borne types of relapsing fever :—

Spanish type	*Louse-borne type*
1. Commonest from May to October.	1. Mainly a winter disease, February and March.
2. Outbreaks small and limited in spread.	2. Often widespread.
3. Usually 4 or 5 febrile periods; rarely 3 or 6.	3. Usually 2 or 3 febrile periods; occasionally only one. (Those with 4 or 5 are probably not louse-borne).
4. Prognosis favourable.	4. Prognosis more grave.
5. Cure often spontaneous; neo-salvarsan ineffective.	5. Neosalvarsan usually quite effective.

There is no real index; the index so-called is merely a detailed list of contents but this is so full that more is hardly needed. As with other books of this series a full or even extensive bibliography is not attempted; but in the list of the most important works consulted it is gratifying to note that special mention is made of the *Tropical Diseases Bulletin* and of the *Transactions of the Royal Society of Tropical Medicine and Hygiene.*

In conclusion, though in paper covers the book is strongly bound and well got up, the illustrations are good and the coloured plates well reproduced; charts and diagrams are clear. The proofs have evidently been very carefully corrected, for we have found no misprints. *H. Harold Scott.*

Das Gupta, B. M. [Professor of Protozoology and Director, Calcutta School of Tropical Medicine]. **Knowles's Introduction to Medical Protozoology.** 2nd Edition, revised and abridged. pp. xviii+323. With 104 illustrations & 10 coloured pls. 1944. Calcutta: U. N. Dhur & Sons, Ltd., 15 Bankim Chatterjee Street, College Square. [Rs. 20/-.]

In 1928, Robert Knowles published in India his Introduction to Medical Protozoology. This work, as the author whole-heartedly admitted, was based very largely on the reviewer's Protozoology, published in England two years before. Knowles's book was intended chiefly for the use of students in India and has been extensively used in that country. In 1936 Knowles died and the task of preparing a second edition has fallen upon his successor in the chair of Protozoology at the Calcutta School of Tropical Medicine, Professor B. M. Das Gupta, who was Knowles's assistant.

The second edition differs from the first in that it is shorter and cheaper, as a result of removal of those sections which are only remotely connected with the subject of medical protozoology. What remains has been thoroughly

revised and brought up to date as regards knowledge acquired since 1928. The result is a book of 323 pages instead of the 887 of the first edition. From the point of view of the student of medical protozoology who needs only information regarding the parasitic protozoa of man, the book offers all that he can want, while sufficient references are made to the allied parasites of animals to indicate that there is a wider field into which he can enter by studying the larger and more comprehensive treatise. It is only natural that frequent references are made to conditions existing in India and in the author's own experience, and as the book is intended primarily for the Indian student this undoubtedly adds to its value. The book is particularly free from mistakes, so that students, whether in India or elsewhere, can rely upon it as giving the latest information on the protozoa which are of medical importance. In some places it would have been possible to give more details, but this would have increased the size of the book, which the author was at pains to avoid.

Apart from the protozoa, descriptions are given of a variety of organisms which students of protozoology are likely to encounter in their work. These come under the headings *Toxoplasma, Rickettsia, Chlamydozoa, Anaplasma, Grahamella, Rhinosporidium, Histoplasma, Cryptococcus, Blastocystis* and Spirochaetes. A final section deals with laboratory methods in a very complete and useful manner. It seems that some of the staining methods which appear in the section on malaria would more appropriately have been included here. However, this is a small matter of little importance. The illustrations are excellent, especially the 10 plates, which as regards detail and colour are distinctly superior to those of the first edition. It seems unnecessary to describe the book in greater detail ; suffice it to say that in the reviewer's opinion the book is a thoroughly good one, which successfully achieves all that the author undertook to carry out. It can be recommended to all those who wish to study the parasitic protozoa of man and the various diseases and pathological conditions they produce. *C. M. Wenyon.*

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